THE BLOOD SUGAR IN OBESITY.

A Survey of the recent literature with an account of the personal investigation of several Cases.

by

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I. INTRODUCTION.

Obesity may be defined as the condition which arises as the result of long continued excess in the amount of food consumed over that metabolised. It becomes pathological as soon as it interferes with functional activity and such interference is bound to come unless the morbid process is arrested.

The condition in its grosser forms, is not at all uncommon; and it is this later gross stage, which I wish particularly to deal with. The type is represented in Literature by such well known characters as "Falstaff" and "the Fat boy" in the Pickwick papers.

When obesity becomes pathological it must be regarded as a serious condition, because it is then that a series of vicious circles develop, and from their effects the disease becomes a self-aggravating and self perpetuating condition which often spells disaster to the sufferer.

To mention only a few of such circles, we have a Cardio-vascular[1] one, with a Fatty Heart, necessarily limiting exercise; through lack of the latter the deposition of fat is aggravated. This circle is probably one of the most important, in fact, Von Noorden[2], states that most stout people die of Cardiac failure, in the long run.

Another/

Another important combination is that associated high blood pressure, arterio-sclerosis, and Chronic Bright's disease[3-4], all of which tell back again on the heart.

The gravity of the condition is yet further emphasized by looking at the records[4] of 120,000 insured persons; there is an excessive death loss on persons whose weight is 20% over the average.

Joslin[5] attached great importance to the fact that "many diabetics were overweight for their age and height when the diagnosis of Diabetes Mellitus was first made, or have a history of Obesity before diabetic symptoms appeared." It was really this statement by such an authority as Joslin, that induced me to investigate the state of the Blood Sugar in the Obese.

Many physicians realise the importance of the condition because of the vicious circle danger and many, in addition, bear in mind its possible relationship to Diabetes Mellitus. From the point of view of logical treatment, it would seem necessary to have some knowledge of the carbohydrate tolerance of the patient, and such knowledge is gained by investigation of the Blood Sugar and its response to the Glucose Tolerance Test.

II. THE GLUCOSE TOLERANCE TEST.

The method which I have personally used in my series of cases, is that of MacLean.[6-7] The blood is obtained from a finger-prick and may be regarded as arterial. Most American workers have used colorimetric methods involving the withdrawal of large quantities of blood from a vein. The curve, according to Forster[8], given by estimations of the Sugar content of blood obtained by venous puncture, is very definitely lower than the curve, plotted simultaneously by determinations of the blood sugar level, obtained from a finger prick; in fact the sugar content of venous blood may be as much as 0.03 to 0.04% lower. In the fasting condition the concentration of the blood sugar in venous and finger prick blood are practically identical.

As the result of this difference in technique, the hyperglycaemia after glucose ingestion, noted in Europe, has been more marked than that met with in America, where Bang's micro-method appears to be very much in vogue.

Before describing the results obtained from Glucose Tolerance Tests in the Obese, I wish to refer briefly to the study of such tests in the normal and in the definitely diabetic subject.

A. THE RESPONSE TO THE GLUCOSE TOLERANCE TEST IN A NORMAL SUBJECT.

The average normal fasting level of the blood sugar is about 0.1 per cent. The limits of normality are between 0.08% and 0.12%. The average normal "Renal Threshold" is in the neighbourhood of 0.18%, but here again we may have individual variations, the normal limits being from about 0.16% to 0.20%.

There is, I think, general agreement[9] about the effect of giving a dose of 50 gm. to 100 gm. of glucose. The Blood Sugar concentration usually rises from the basal figure of, say, 0.10% to a maximum of 0.16% or 0.17%, which is generally reached in 30-60 minutes. There are naturally slight variations depending on absorption rate and other factors. This maximum concentration is only maintained for a few minutes, and then it falls till at last it is slightly lower than the original fasting level. The time for this fall is approximately equal to the time taken for the Blood Sugar to rise to the maximum concentration.

This sudden fall is due to the sudden intervention of a storage mechanism which abstracts sugar from the blood more rapidly than it enters, and as a result masks the later stages of absorption. This mechanism comes into action when the blood sugar reaches 0.16% or/

Blood Sugar

1. ·103
2. ·142
3. ·173
4. ·128
5. ·095

Urine

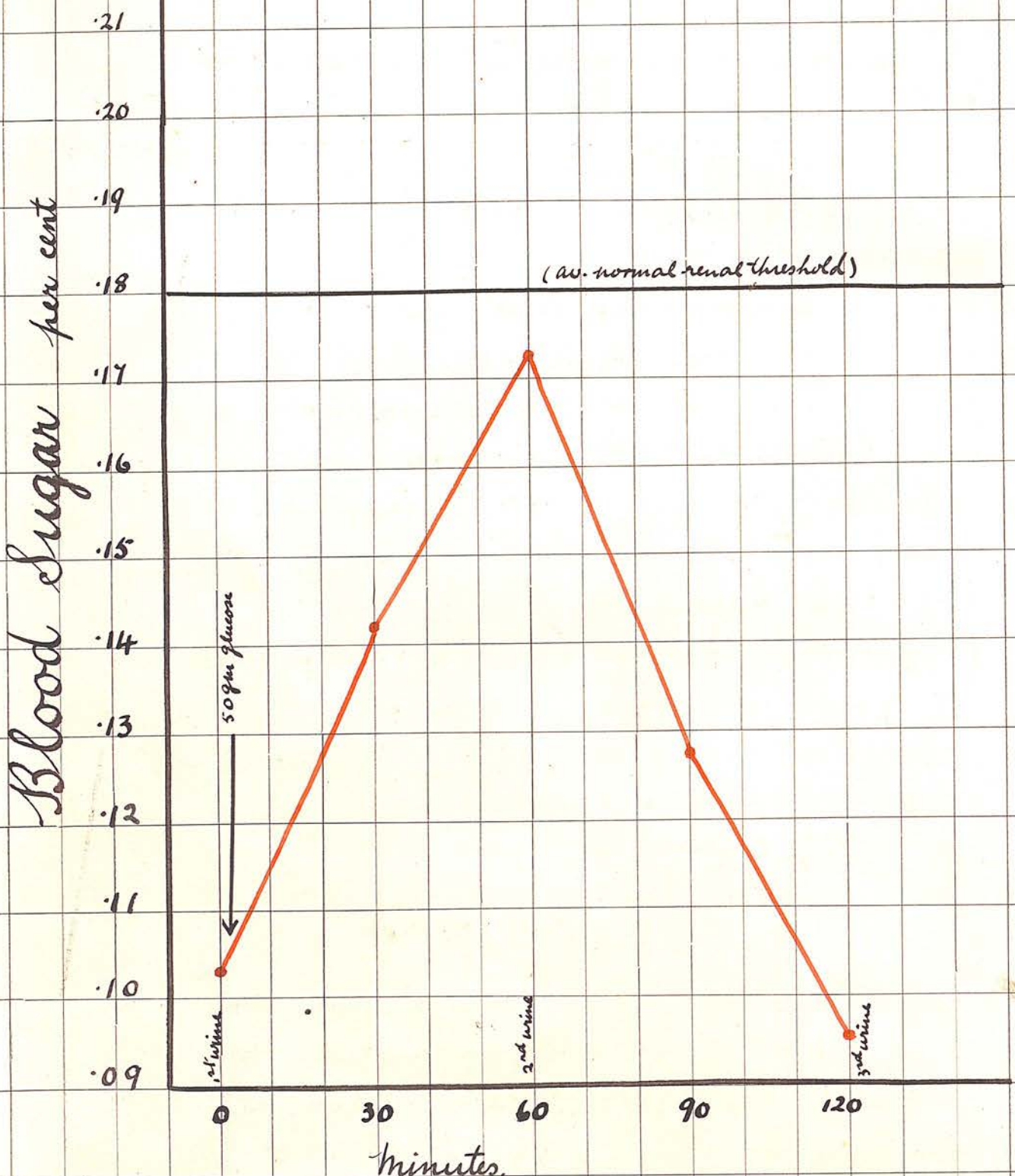
1. 7 –
2. 7 –
3. 7 –

(1) Tm. Tm.

Royal Infirmary

25.2.25.

Normal Curve



or 0.17%, and it is interesting to note that this is just about the point where the kidneys begin to excrete sugar.

Oxidation[10] is another factor in the fall of the Blood Sugar Curve. But the amount of the carbohydrate dealt with in this way is only about 18% of the Total Carbohydrate ingested, so that oxidation is not the main cause of the fall.

This storage mechanism is so efficient that it is difficult, in fact, according to Taylor[11] and Hulton, impossible to force the blood sugar above the Renal Threshold however large an amount of carbohydrate is ingested. Contrary to general opinion, a dose of 200-300 gms. glucose will seldom produce glycosuria in the normal subject, though it may prolong the period during which the blood sugar is abnormally high.

Fig I is the curve obtained after the ingestion of 50 gm. glucose in a normal subject. It illustrates all the points referred to above.

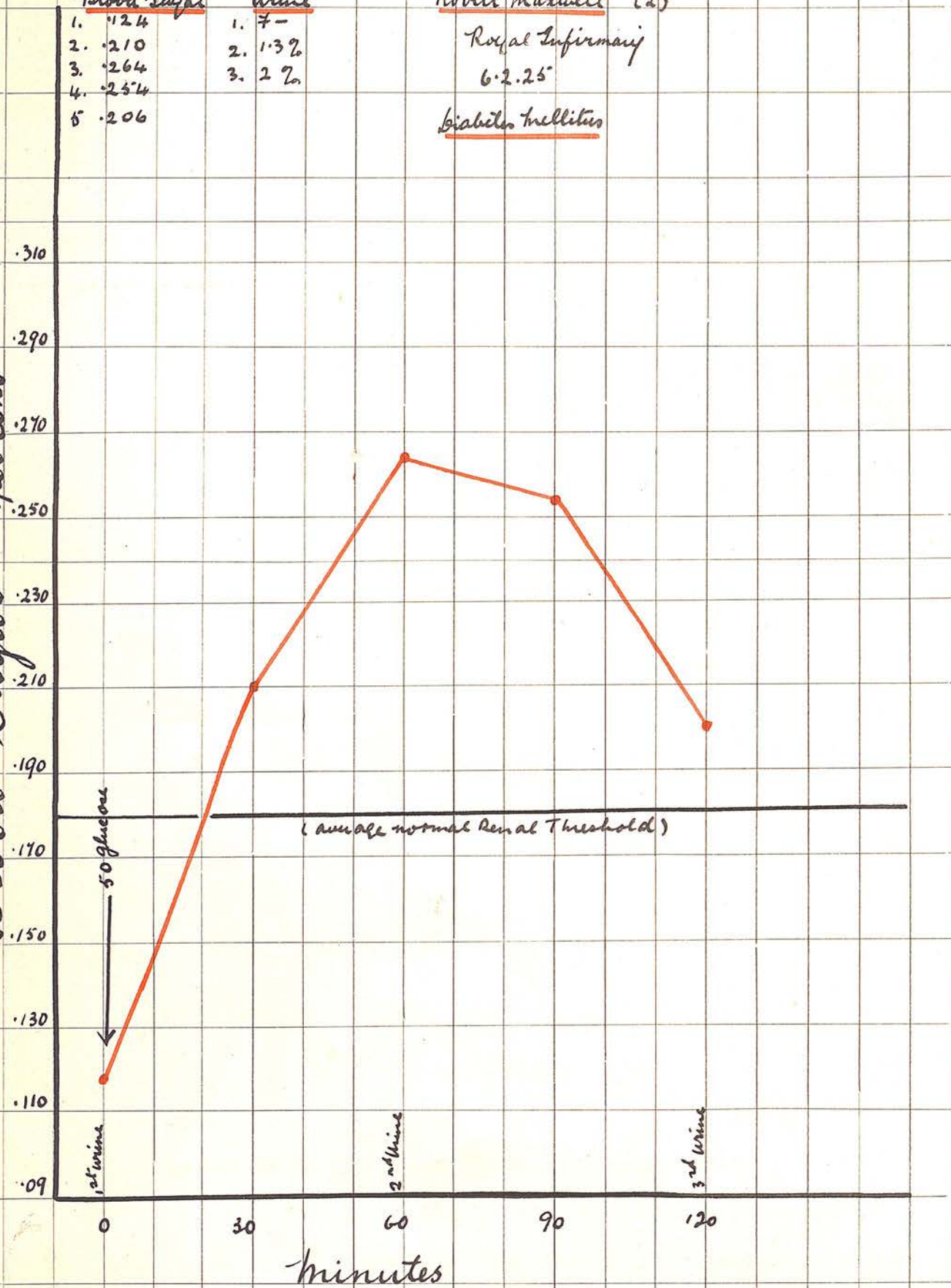
B. THE DIABETIC RESPONSE.

Now let me refer for a momentto the type of response obtained in a Diabetic after ingestion of 50 gm. glucose. The graph of Case No.2 is shown, as being fairly typical. Note that it differs from Case 1 in three[12] important respects.

(1)/

Blood Sugar	Urine
1. ·124	1. 7–
2. ·210	2. 1·3%
3. ·264	3. 2%
4. ·254	
5 ·206	

Robert Maxwell (2)
Royal Infirmary
6·2·25
Diabetes Mellitus



(1) High Fasting level.

(2) Hyperglycaemia "overshoots" Renal Threshold.

(3) * Prolonged curve - no return to Fasting level after 2 hours.

The last point is the most important as this prolongation is constantly present in early mild cases of Diabetes Mellitus, in spite of the fact that the fasting level is within normal limits and that no overstepping of the Threshold is present.

Notice further that considerable glycosuria was present, through the Blood Sugar overstepping the "leak" point of the kidney. This case had also, considerable polyuria during and after the test.

III. THE BLOOD SUGAR IN OBESITY.

A. A SURVEY OF THE ASSOCIATED LITERATURE.

While a great deal has been written upon the subject from a purely clinical standpoint, there has been comparatively little work done on the blood sugar findings. What has been done, has been confined to the last seven or eight years, and the object, in many instances, was an attempt to clear up the relationship of Obesity to Diabetes Mellitus.

We/

We have already mentioned Joslin's[5] statement that many Diabetics at the onset of the disease were very obese, and that many obese persons subsequently became diabetics. Von Noorden[13] followed, for a long time, the course of 15 obese patients, and found that 5 of them developed Diabetes Mellitus later. It has also been noted by MacLean[14], Aldren-Turner[15], De Wesselow[16], Herrick[17], and Rosenraad[18], that glycosuria was present in many obese people, either permanently or only at certain periods. This would make us think at once of the possibility of Diabetes Mellitus being present, though of course, glycosuria is not synonymous with that condition. Rosenraad goes as far as to say that glycosuria is present in 50% of obese subjects. Preble[19], as a result of the examination of 1000 obese patients found that 75 showed glycosuria. This was found out in the ordinary routine examination, no glucose tolerance test being done. According to Joslin[20] one in every hundred of the population has or may develop Diabetes. The above figures show an incidence of glycosuria and, according to Preble, "presumably of diabetes" of over 7½ times this normal figure.

Now let us look at the Literature dealing with the Blood Sugar of the obese subject and its reaction to the Glucose Tolerance test. I refer more particularly to the ordinarily obese subject and not so much to/

to the type seen in a Fröhlich's syndrome. I shall however mention, shortly, at a later stage, the present state of our knowledge of the Blood Sugar in that condition.

Beeler and Fitz[21] investigated 32 cases who had come to the Mayo Clinic for obesity alone or for obesity and some secondary condition that could not be related to Diabetes. Their urine was, in every case, sugar free.

One of the men weighed 370 lbs., one 285 lbs., one 253 lbs. and the others were at least 10% overweight for their age and height. The heaviest woman weighed 291 lbs., several others were more than 225 lbs., and the rest were all 10% or more overweight according to medico-actuarial statistics[22].

Glucose Tolerance Tests were done according to the plan of Hamman and Hirschman. The following are the average results of the Blood Sugar findings, compared with those of non-diabetic and mild diabetic controls.

Time	Obese	Mild D.	Non D.
½ hr.	.120	.10	.90
1 hr.	.20	.170	.160
2 hr.	.28	.180	.14
3 hr.	.285	.160	.120
4 hr.	.220	.120	.90

The curve for the obese patients shows a position midway between the two, although it approaches to the normal more closely than to the diabetic. These results are, however, only the average over 32 subjects.

If the cases are taken separately we find that 4 had a fasting Blood Sugar level above 0.15%; 2 of these had a normal Blood Sugar curve in other respects; and the other 2 gave a reaction to the glucose tolerance test so typical of diabetes mellitus that it was certain that they represented an early stage in the disease.

Six patients while having a Fasting Blood Sugar content of 0.12% or less, had a persistent hyperglycaemia following the ingestion of glucose, and thus resembled mild diabetes in their type of reaction. Average readings at same time intervals as above were 0.12, 0.20, 0.28, 0.29, 0.25. The urinary findings will be referred to later.

The majority of persons observed had no fasting Hyperglycaemia and had a nearly normal Blood Sugar curve following the ingestion of 100 gm. glucose. It is probable however that more striking results could be obtained if the dosage of glucose were made on the basis of body weight and if the sugar solution were given intravenously after the method of Woodyat, Sansum and Wilder.[23]

The excretion of Sugar by the obese patients was

of/

of two types; 11 excreted normal or subnormal amounts after ingestion of 100 gm. glucose and 6 patients excreted an abnormally large amount.

With two exceptions all the patients who excreted small amounts had a normal Blood Sugar Curve. The two remaining patients had a diabetic type of glycaemia so that in one case the last reading was 0.25%. There was no evidence of Renal impermeability in these cases.

Those patients who excreted abnormally large amounts of sugar after ingestion of 100 gm. glucose all had a blood sugar curve like mild diabetics. Beeler and Fitz say that such people should be treated as diabetics.

Generally speaking those patients with a normal blood sugar curve and no glycosuria voided small volumes of urine, while those with a diabetic type of curve and an increased excretion of sugar, voided a large volume of urine. Labbé[24] states that this is due to chloride retention, but, according to Graëfe[25], it is due to an interference with the Thyroid mechanism for regulating intra-cellular water metabolism.

Let me briefly summarise the findings, then, of Beeler and Fitz. Obese people show changes in sugar and water metabolism, and fall into two groups. The first group is characterised by a relatively normal response to the Glucose Tolerance test by the blood sugar, and the excretion of small volumes of urine and/

and small amounts of sugar. This group will not develop Diabetes Mellitus.

The other group shows a Blood Sugar curve like that of a mild diabetic, along with the excretion of large amounts of sugar, and some may have also a slight diuresis. This group is probably pre-diabetic and should be treated on anti-diabetic lines.

Herrick[17] investigated the association of high blood pressure with hyperglycaemia, in a series of cases extending over several years. He formed the opinion that the majority of the cases belonged to a definite group, characterised by the four cardinal features of Hypertension, Hyperglycaemia, Obesity, and Arteriosclerosis. Hyperglycaemia occurs in 10-30% of all cases of high blood pressure. He states that, while it does occur, it is exceptional to find hyperglycaemia in thin persons associated with hypertension.

This group he calls the "Essential Hypertonias", as it does not include the examples of hypertension that are associated with other definite conditions such as Kidney insufficiency, Aortic leakage, Toxaemias of pregnancy, intra-cranial conditions, etc. Herrick knows of no experimental work that has been done in relation to hyperglycaemia and hypertension. The work which has been done is based entirely on Clinical observations.

In/

In the group referred to, the reduction of the Hyperglycaemia to a normal level and its maintenance there, is followed by a fall in blood pressure. This is probably due, merely, to the reduction in body bulk, which quite constantly follows the dietary regulation of high blood sugar in the obese hypertonic patient. This reduction of weight in obese persons with hypertension and hyperglycaemia, is a much simpler and easier matter than reduction in weight of a similar person with a normal or a low Blood Sugar level.

The hyperglycaemia appears to be more common where the high blood pressure is not associated with obvious disease of the Kidneys. Prolonged hyperglycaemia may cause arterio-sclerosis and still further raise the blood pressure.

W.E. Preble[19] carried out investigations on the blood sugar in 31 obese subjects without Diabetes mellitus or Chronic Nephritis. These patients all had a light breakfast and the blood sugar was estimated 3 hours or more later. The figures lay between 0.82% (low) and 0.125% (high), all inside normal limits. He also found that the N.P.N. figures were also within normal limits. The methods used in Blood Analysis were those of Folin and Wu[26].

Wilder and Sansum[27] reported on the Sugar Tolerance of a few cases of obesity, which were studied by using continuous intra-venous injections. They found no/

no increased tolerance by this method, in these cases, and suggested that the increased tolerance of such cases for sugar, was really due to delayed absorption from the bowel rather than to any anomaly of intermediate metabolism.

Roth[28] found the sugar of the blood decidedly above normal in 4 out of 16 cases of obesity examined by him. Glycosuria followed the ingestion of 100 gm. glucose in only 3 out of the 4 cases, but examination of the sugar concentration of the blood revealed the "latent Diabetes" in all 4 cases. He urges anti-diabetic treatment in such cases as warding off diabetes and curing the obesity. He also points out the ill effects of arteriosclerosis, Bright's disease, etc. Bang's micro-method was used in all cases.

De Wesselow[16] states that the association of obesity and Glycosuria is well known. He thinks that a considerable number of obese patients show a blood sugar curve suggestive of a mild degree of impairment of carbohydrate tolerance and that in some glycosuria appears after the ingestion of 100 gm. glucose. He advises that such patients should be treated as potential diabetics.

THE BLOOD SUGAR IN HYPOPITUITARISM.

I wish to make a brief reference to the state of our knowledge of the Blood Sugar in this condition, as a/

a few cases of obesity can be classified under this head.

The work of Blair Bell[29] and Cushing[30] have done a great deal in improving our knowledge of the subject. While they may differ from each other as to which lobe is at fault, they are agreed, that in this condition there is a great capacity for warehousing sugar. The response to the ingestion of glucose is very small, only amounting to 0.02% or 0.03% in some instances. Huge amounts of glucose do not cause glycosuria. Crosser Griffith[31] demonstrated increased Sugar tolerance in a case of Hypopituitarism. One hour after ingestion of 100 gm. glucose the blood sugar was 0.104% with no glycosuria. After two months treatment with pituitary extract, sugar tolerance decreased and after 100 gm. glucose the curve rose to 0.18% in 1 hour and sugar was passed.

More recent work by Janney and Isaacson[32] and by Zloczower[33], however, suggests that, although most cases show a great capacity for warehousing sugar, associated with a flat curve, there is a type which shows a very high and sustained curve. Such cases are clinically identical with the ordinary case of Fröhlich's.

Sansum and Wilder[27] used the continuous intravenous method in studying the blood sugar in 5 cases of Hypopituitarism. They, as before in a few ordinary cases of obesity, found that there was no increased tolerance/

tolerance by this method and suggested that the increased tolerance was really due to delayed absorption from the alimentary tract and not due to any anomaly of intermediate metabolism.

In the "Obesity" seen in Myxodema the sugar tolerance is variable[34]. It may be increased or decreased. The renal threshold for sugar is usually raised in Myxodema and consequently glycosuria does not follow. In Cretins, on the other hand, increased tolerance seems to be a constant finding.

B. AN ACCOUNT OF THE PERSONAL INVESTIGATION OF SEVERAL CASES OF OBESITY.

The following series of cases were investigated by me in the medical wards of the Royal Infirmary, Edinburgh, and of Leith General Hospital. MacLean's[12] method was used in all cases. To ensure accuracy my results were controlled by the Royal College of Physicians Laboratory, Edinburgh, in every instance; and in many cases by the Royal Infirmary laboratory as well. The blood sugar estimations in those cases from Leith Hospital, were carried out in the Royal College of Physicians laboratory alone, as I had not the necessary apparatus and solutions at hand.

The/

The dosage[35] of Glucose given was 50 gm. in 150 cc. water, flavoured with Lime Juice to prevent nausea. In every case no food had been taken since 7 p.m. on the previous evening. Such a dosage, according to MacLean, is ample for all purposes, for he sees no advantage in giving a dose of 100 gm. A sample of "fasting" blood was first taken. This was followed up immediately by the glucose and the blood samples were taken at ½ hour intervals, thereafter until 2 hours had passed.

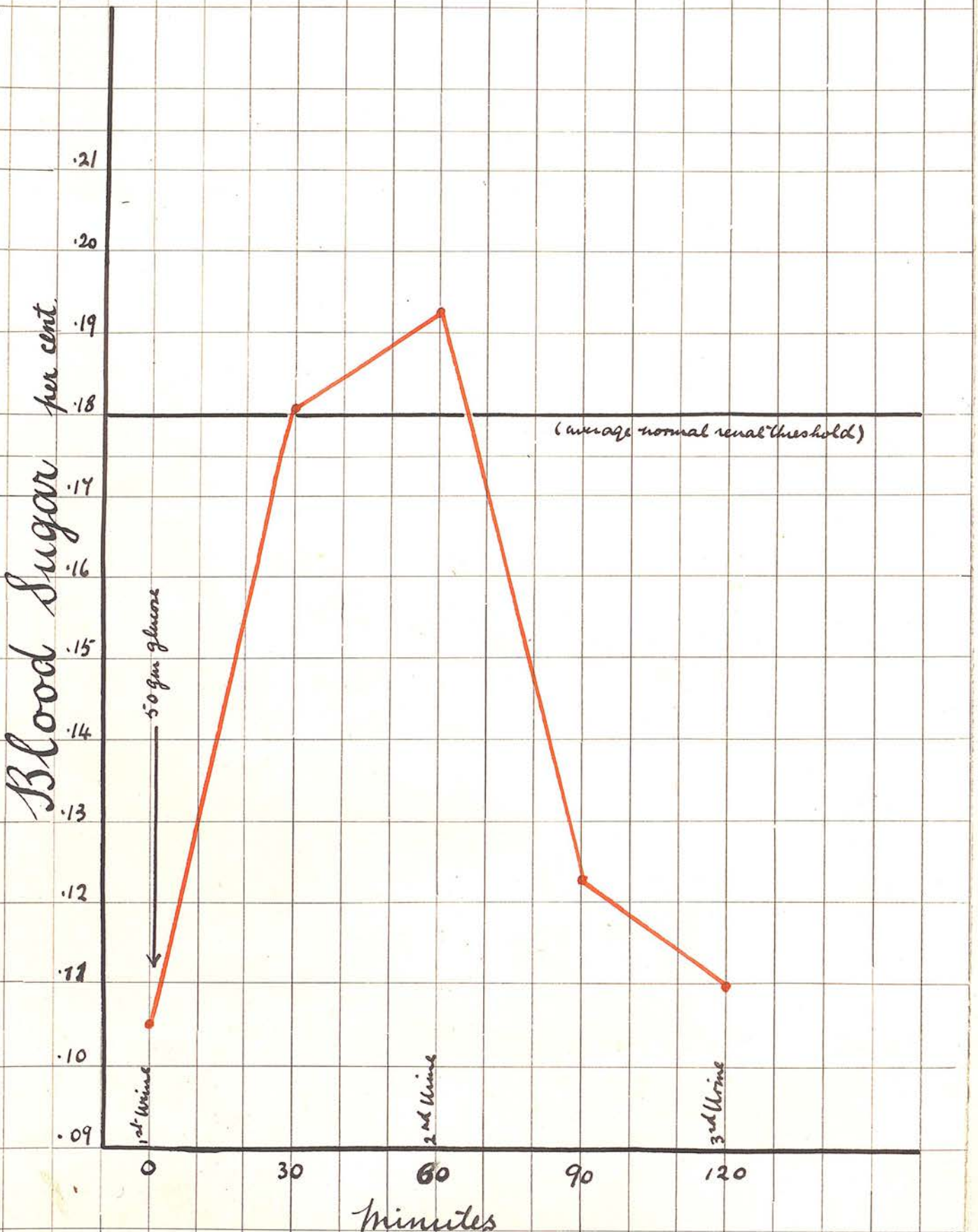
As all my cases were females it was found to be inconvenient to obtain urinary specimens at ½ hour intervals. They were therefore procured immediately prior to the test, and at intervals of 1 hour and 2 hours after the ingestion of the glucose.

The qualitative testing was done by freshly prepared Fehling's solution; the quantitative estimations of sugar were usually done by Benedict's method, though in several instances Bertrand's[36] method was used. The latter method was particularly useful in estimating the smaller amounts of sugar. Its usefulness lies in the very definite end point.

I shall group the cases in a certain order, to be explained later. A few clinical notes from the case records are also appended.

Blood Sugar	Urine
1 ·106	1 7-
2 ·181	2. 7-
3 ·193	3. 7-
4 ·123	
5 ·110	

Mrs Mary Barron
Leith Hospital
15.4.25.
Obesity



GROUP I.

Case No.3.

Mrs Mary Barron. Leith Hospital.

Aet. 51. 15.4.25.

Weight 11 st. 10 lb. 8 oz. = 165 lbs.

Height 5 ft. 4 in.

Normal for age and height = 137 lbs.

Systolic Blood pressure 183 mm.

Diastolic " " 120 mm.

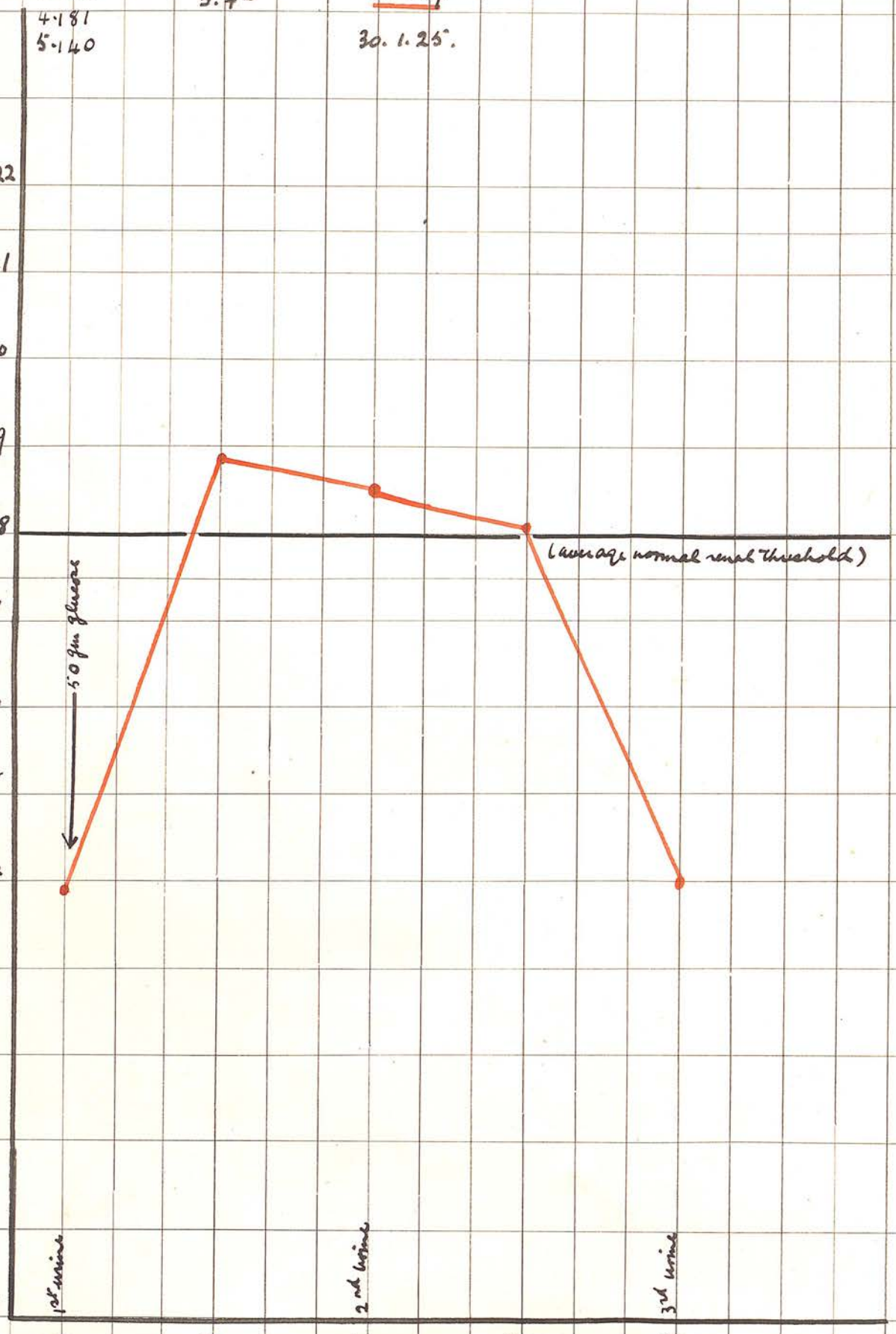
Clinical Record:- Pulse 74.- Respirations 20: Dyspepsia, pain in right hypochondrium, no tenderness, doubtful history of malaena, vague stomach symptoms. Test meal showed hyperacidity. 4 children living and 1 miscarriage. Says she has got much fatter since the menopause, which in her case, occurred 8 years ago. Gets up once per night to make water. Diagnosis uncertain, between Duodenal ulcer and Gall-stones.

Blood Sugar.

Time	0	30	60	90	120	Minutes.
Urine	-		-		-	Fehling's
B.S.	.106	.181	.193	.123	.110	Gm.%

Blood Sugar	Urine
1. ·139	1. 7-
2. ·189	2. 7-
3. ·186	3. 7-
4. ·181	
5. ·140	

Mrs Siddons
Royal Infirmary.
Glycosuria
30. 1. 25.



The curve is comparatively normal, though the apex is above the "average" Renal Threshold. It is not far above it however, and cannot be considered abnormal as thresholds vary[37] in individual cases, the limits of normality being between 0.17% and 0.20%. The fall of the curve is sharp and the fasting level is regained in the normal time, i.e. 2 hours. There was no glycosuria throughout the test.

Case No.4.

Mrs Siddons. Royal Infirmary.

Aet. 45. 30.1.25.

Height 5 ft. 4 in.

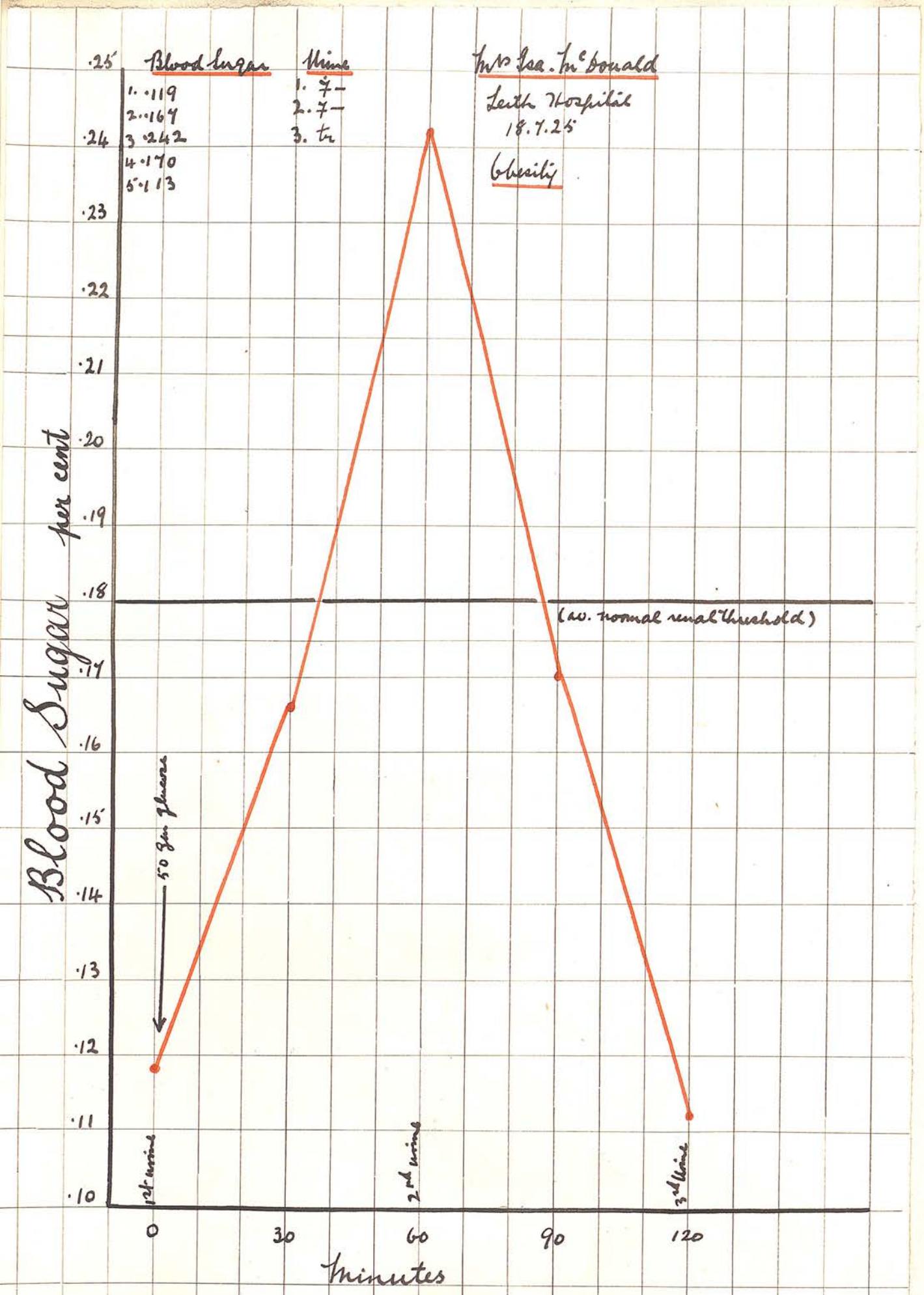
Weight 10 st. 5 lbs. = 145 lbs.

Normal for age and height = 135 lbs.

Clinical record:- Aortic incompetence, syphilitic cirrhosis of liver. History of alcoholism. Abnormal constituents in urine, albumen trace.

Blood Sugar.

Time	0	30	60	90	120	Minutes
Urine	-		-		-	Fehling.
B.S.	139	189	186	181	140	Gm. %.


Blood sugar
Urine
1. -119
2. 164
3. 242
4. 170
5. 113
1. ÷
2. -
3. tr
Mrs Jas. McDonald
Leith Hospital
18.7.25
Obesity
.25
.24
.23
.22
.21
.20
.19
.18
.17
.16
.15
.14
.13
.12
.11
.10
Blood Sugar per cent
(av. normal renal threshold)
50 gm glucose
1st urine
2nd urine
3rd urine
0
30
60
90
120
Minutes

Fasting level is rather on high side, possibly due to a raising of the renal threshold by the associated Nephritis (see later). The apex of the curve is again above the "average" renal threshold but yet it is not so far above to be called definitely abnormal. The storage mechanism therefore appears to be functioning normally.

Case No.5.

Mrs Isabella MacDonald. Leith Hospital.

Aet. 46. 18.7.25.

Weight 166 lbs.

Height 5 ft. 2 ins.

Normal weight for age and height = 130 lbs.

Clinical record:- Pulse 74. Respirations 20. No abnormal constituents in urine. 19 pregnancies; abortion 3 weeks prior to admission. Puerperal fever 3 years ago. Menorrhagia. Blood picture was that of a secondary anaemia. Pulmonary systolic; soft mitral first sound; tiredness and dyspnoea on exertion. Diagnosis secondary anaemia.

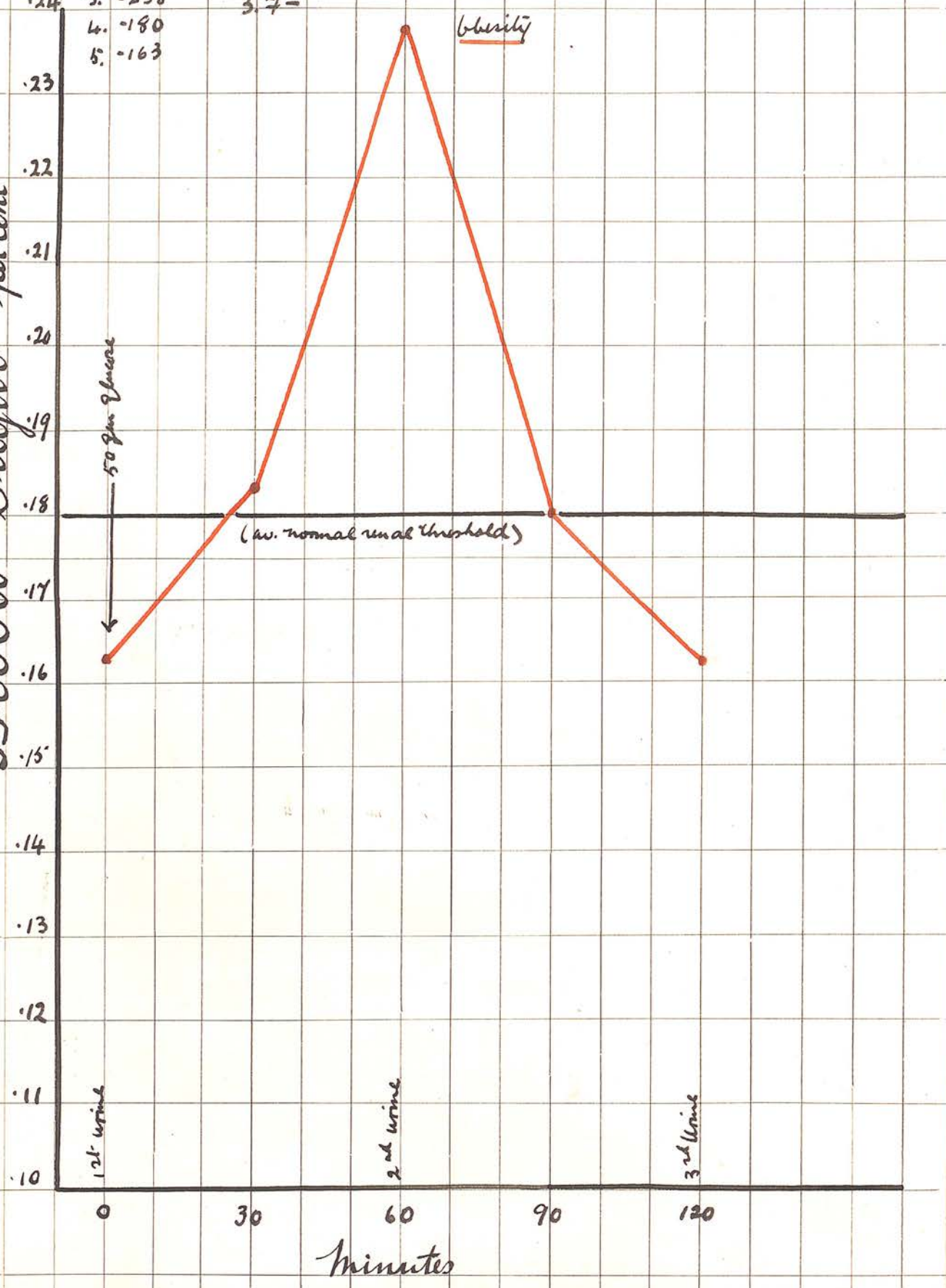
Blood Sugar.

Time	0	30	60	90	120	Minutes.
Urine	-		-		tr.	Fehling's
Blood	.119	.167	.242	.190	.113	Gm. %

Blood sugar	Urine
1. ·163	1. 7–
2. ·183	2. 7–
3. ·238	3. 7–
4. ·180	
5. ·163	

Mrs A. Cormack
Leith Hospital
24.7.24

Obesity



This curve differs from those preceding only in the height to which it rises. Note particularly that it regains the fasting level in the normal time. It appears to conform to the "Lag" type of curve, described by MacLean[38]. In such a curve the storage mechanism is for some reason, late in coming into action: when it does however it functions very powerfully so as to reduce the level to normal again inside the usual period. It is not to be regarded as a prediabetic curve and is of no significance.

Case No.6.

Mrs Anabella Cormack. Leith Hospital.
Aet. 38. 24.7.25.
Weight 21 st. = 295 lbs.
Height 5 ft. 2 in.
Normal for age and height = 144 lbs.

Clinical Record:- Profound dropsy and much albuminuria. Intense dyspnoea and cyanosis. Effusion into both pleural sacs, and ascites. Heart sounds very faint. Crepitations at both bases. Insomnia and delirium at night. Alcoholic history. Systolic blood pressure 260 mm. Diastolic blood pressure 160 mm.

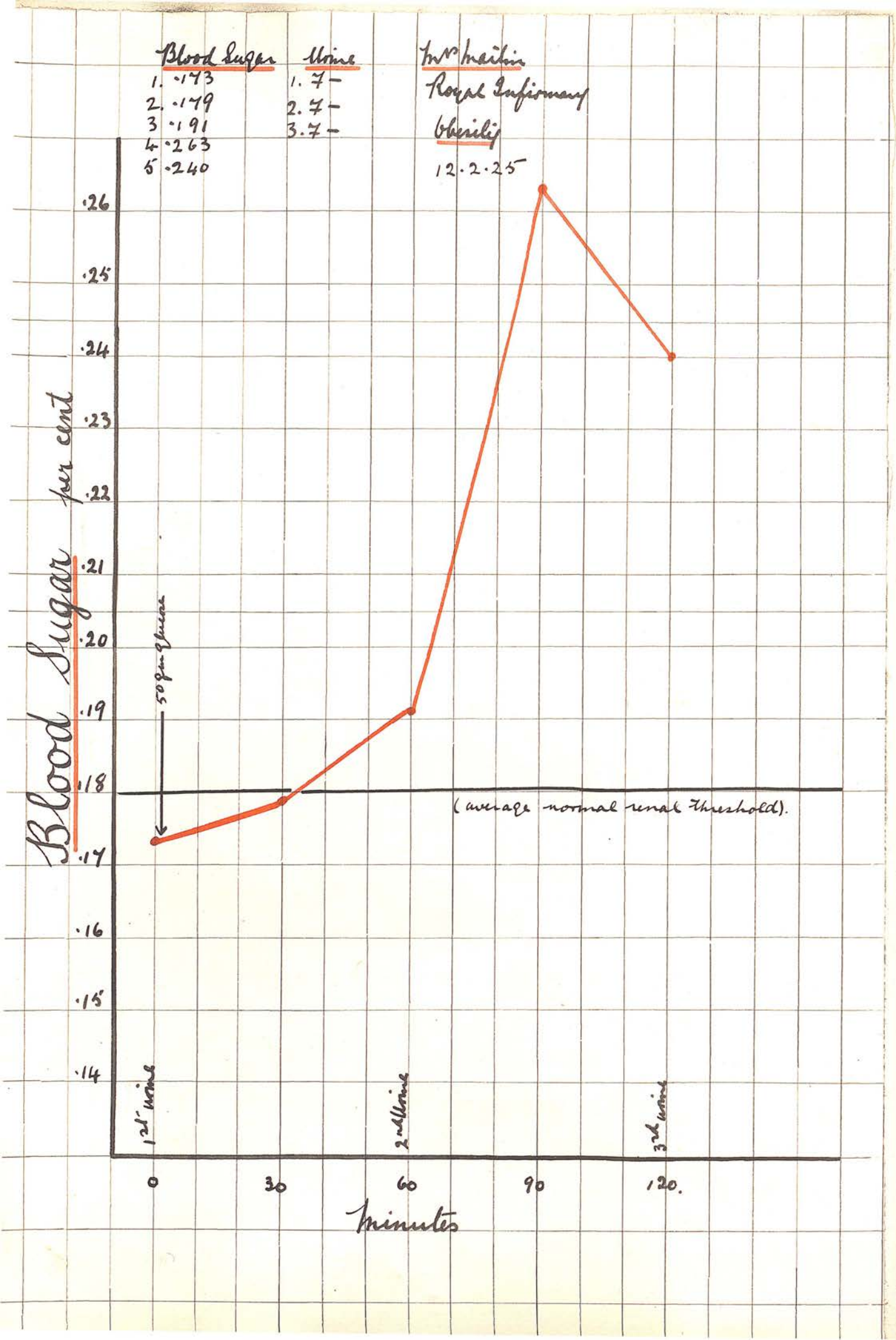
Blood Sugar.

Time	0	30	60	90	120	Minutes
Urine	-		-		-	Fehling's
B.S.	.163	.183	.238	.180	.163	Gm. %

This case gave a history of obesity before the onset of the nephritis. Her bulk was huge and she was sodden with fluid. The fasting level is high, as is also the last reading. The return to the fasting level is accomplished in the normal time. Beyond these two high basal levels the response is normal in other respects. This high fasting level is quite a common[39] finding in nephritis. The absence of glycosuria means a raised renal threshold. The storage mechanism appears to be functioning quite well. The fasting hyperglycaemia may be a temporary condition arising from the nephritis.

Blood Sugar	Urine
1. ·173	1. 7–
2. ·179	2. 7–
3 ·191	3. 7–
4 ·263	
5 ·240	

Mrs Martin
Royal Infirmary
Obesity
12·2·25



GROUP II.

Case No.7.

Mrs Martin. Royal Infirmary.

Aet. 60. 12th Feb. 1925.

Height 5 ft. 4 in.

Weight 15 st. = 210 lbs.

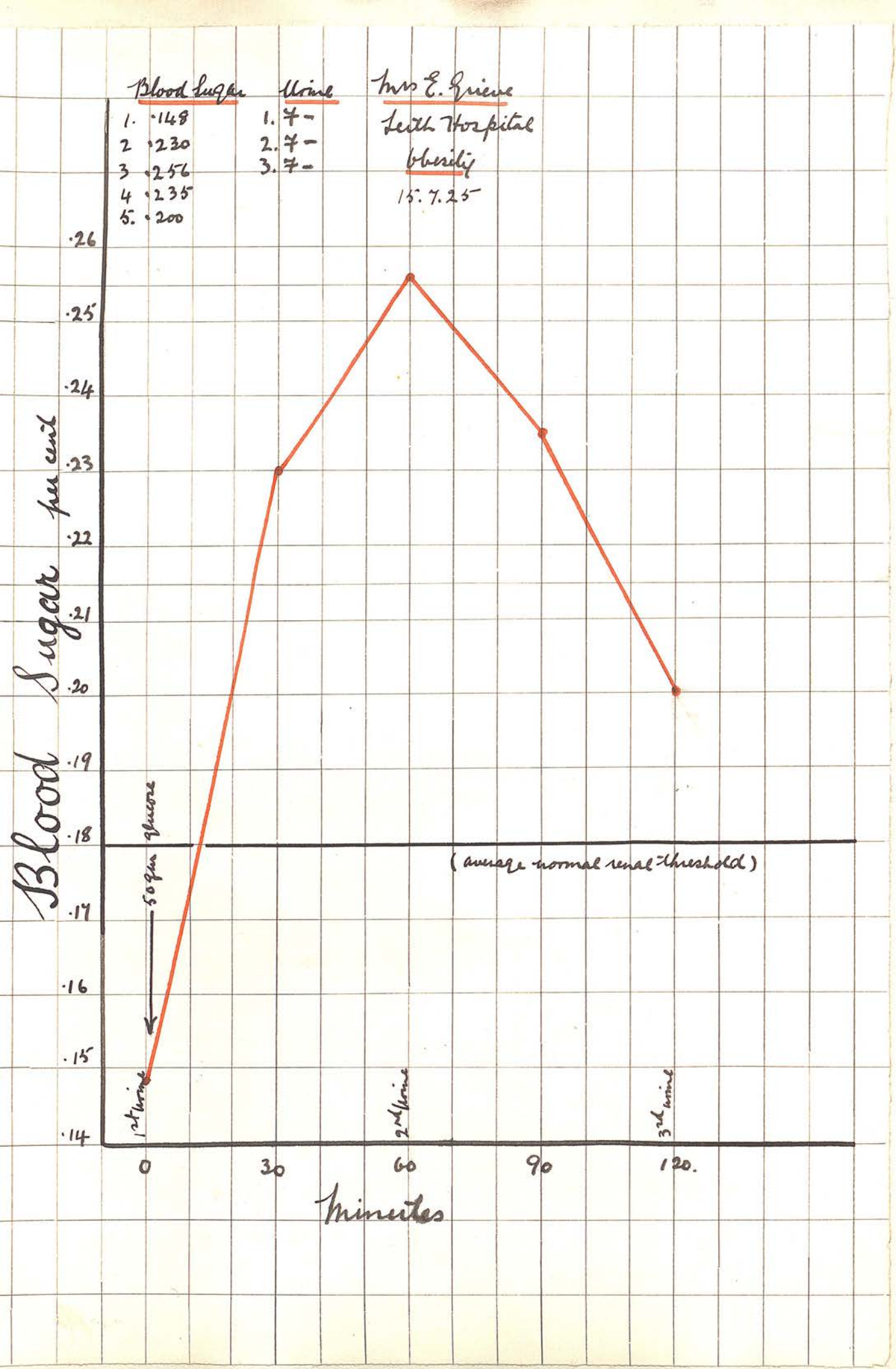
Normal weight for age and height = 140 lbs.

Clinical record:- Patient was not normal mentally, always had inane smile. At times she would not speak and gave foolish answers to any ordinary question. Her age would be 18 one day and 75 the next, and so on. She had a good deal of albuminuria. Pulse was slow and of high tension. Systolic Blood pressure 200 mm. Diastolic 150 mm. Multipara.

Blood Sugar.

Time	0	30	60	90	120	Minutes.
Urine	-		-		-	Fehling's
B.S.	.173	.179	.191	.263	.240	Gm. %.

The points to note in this curve are the original high fasting level, the rising of the hyperglycaemia to 0.263% and slow fall with failure to regain the original level in the normal 2 hours. There was no glycosuria, probably from a raising of the renal threshold. The curve is diabetic in type and points to some deficiency in carbohydrate tolerance.


Blood Sugar
1. ·148
2 ·230
3 ·256
4 ·235
5. ·200
Urine
1. 7-
2. 7-
3. 7-
Mrs E. Grieve
Leith Hospital
Obesity
15. 7. 25
Blood Sugar per cent
·26
·25
·24
·23
·22
·21
·20
·19
·18
·17
·16
·15
·14
50 gm glucose
(average normal renal threshold)
1st urine
2nd urine
3rd urine
0
30
60
90
120.
Minutes

Case No.8.

Mrs Eliz. Grieve. Leith Hospital.

Aet. 51. 15.7.25.

Weight 11 st. 12 lbs. = 166 lbs.

Height 5 ft. 4 in.

Normal for age and height = 138 lbs.

Blood pressure - Systolic 160 mm. Hg.

Diast. 120 " "

Clinical Record:- Vague abdominal symptoms. Nothing to be made out on physical examination. Test meal normal. Mental condition abnormal. Slow development of left-sided Hemiplegia. Double incontinence. Heart normal: vessels palpable. Wassermann - . History of similar attack several months prior to admission. Required to make water during night at least once. Died. Diagnosis - Cerebral Thrombosis.

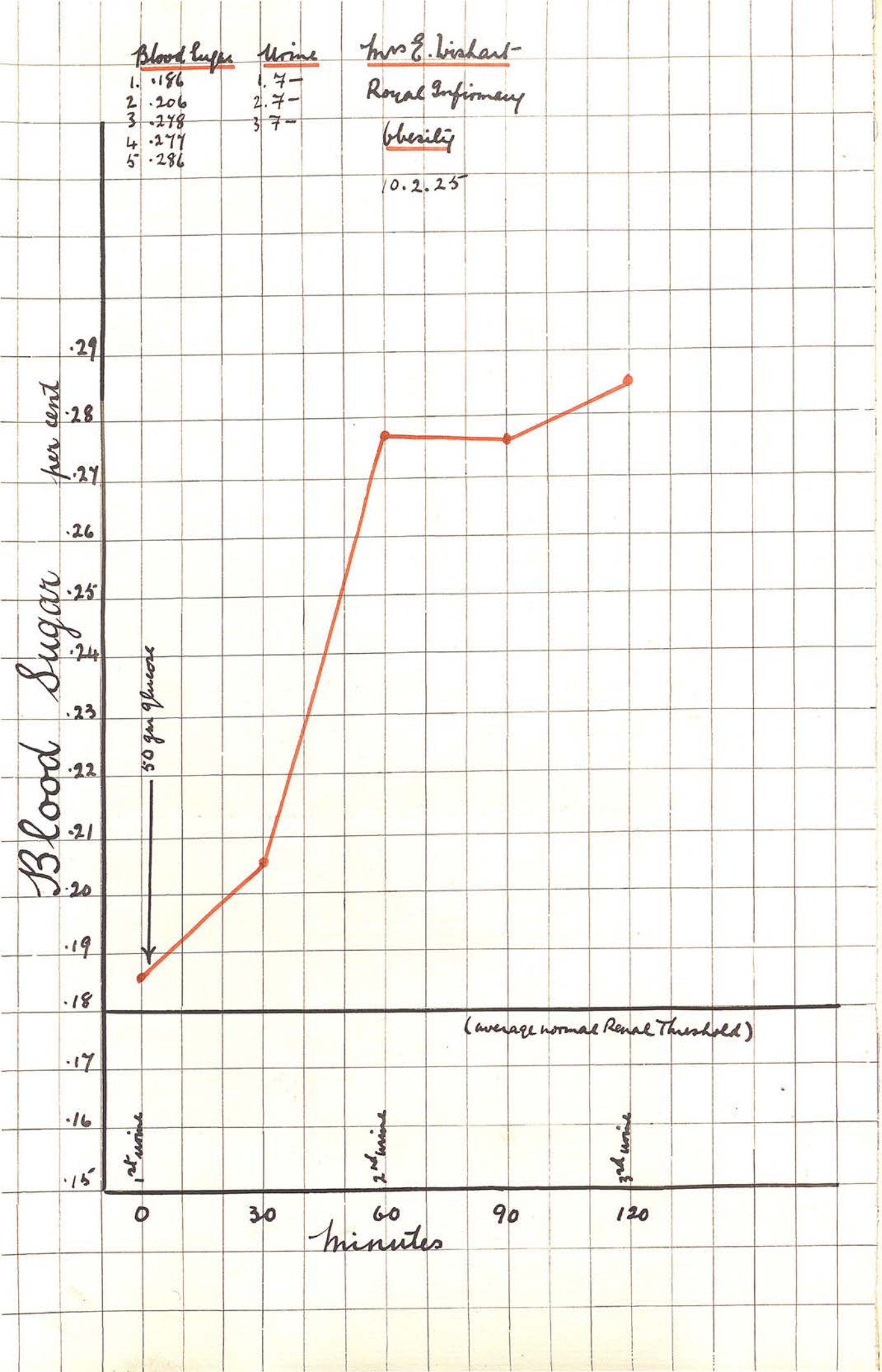
Blood Sugar.

Time	0	30	60	90	120	Minutes.
Urine	-		-		-	Fehling.
B.S.	.148	.230	.256	.235	.200	Gm. %.

This curve is essentially similar to the previous one, i.e. rather high fasting level, overshooting of threshold, and slow fall. Points to certain degree of decreased Carbohydrate tolerance. Note again the absence of Glycosuria.

Blood Sugar	Urine
1. ·186	1. 7–
2. ·206	2. 7–
3. ·278	3. 7–
4. ·277	
5. ·286	

Mrs E. Lishart-
Royal Infirmary
Obesity
10.2.25



Case No.9.

Mrs Elizabeth Wishart. Royal Infirmary.
Aet. 44. 10th Feby. 1925.
Height 5 ft. 1 in.
Weight 17 st. 10 lbs. - 248 lbs.
Normal for age and height - 124 lbs.

Clinical Record:- Complained of pain in stomach and "wheezing". Had persistent cough for 7 years. Breathlessness on exertion; asthmatic attacks every morning. 9 children. Patient was extremely fat, and cyanosed. Was lying propped up in bed. Rhonchi of all pitches heard on both sides. As regards cardio-vascular system, she has complained of great dyspnoea on exertion, and occasional fainting turns. Heart sounds closed and no increase of dullness could be made out. Pulse was full and bounding. Systolic Blood Pressure 155 mm. Diastolic 108 mm. She gave a history of nocturnal frequency of micturition; no abnormal constituents were found in the urine.

Blood Sugar.

Time	0	30	60	90	120	Minutes
Urine	-		-		-	Fehling.
B.S.	.186	.206	.278	.277	.286	Gm. %.

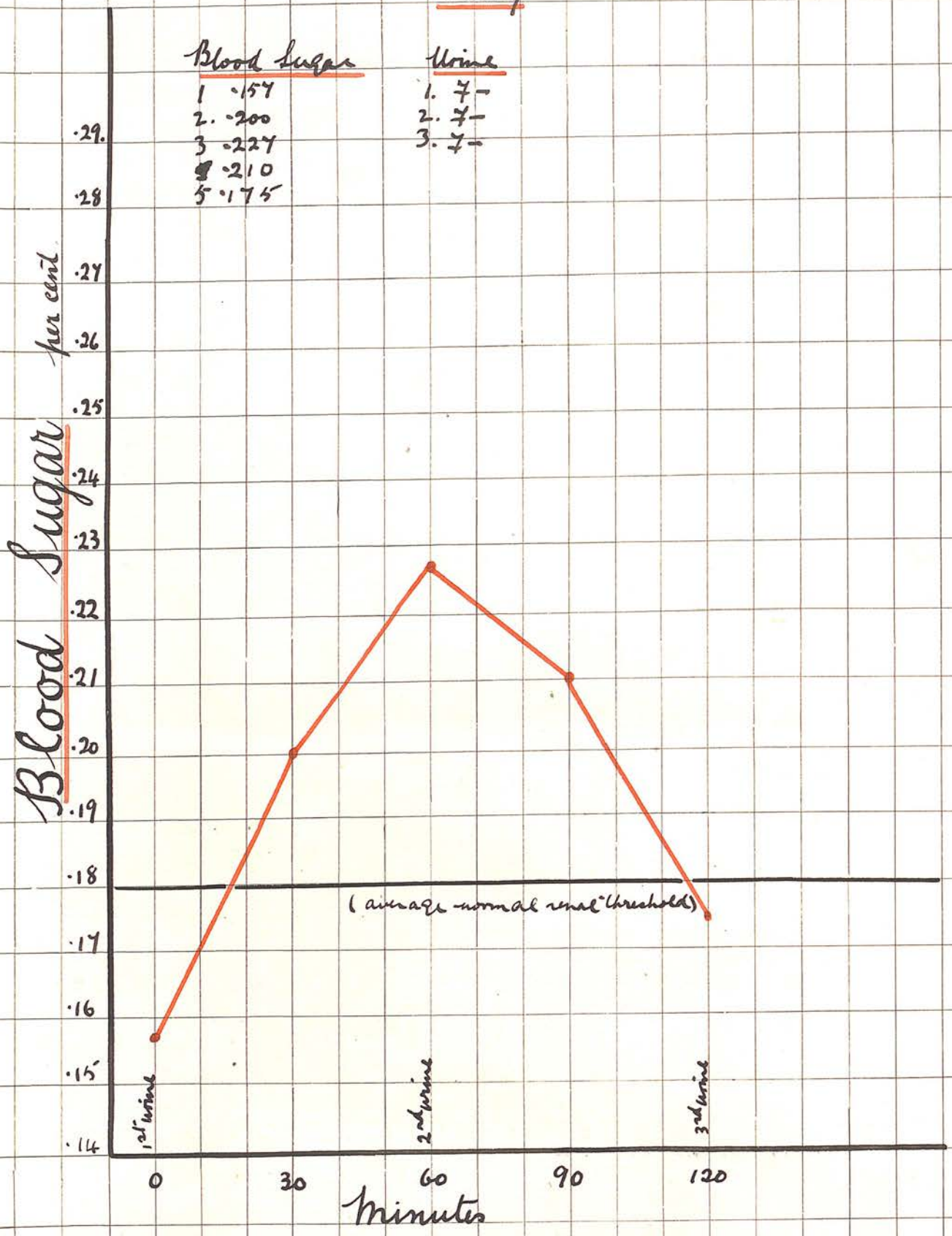
The same features, as are shown in the preceding curves, are present in this curve. The carbohydrate tolerance is impaired, though the urinary examination gives no clue.

Mrs Thom

Leith Hospital 20.8.25.

Obesity

Blood Sugar	Urine
1 ·154	1. 7-
2. ·200	2. 7-
3 ·227	3. 7-
4 ·210	
5 ·175	



Case No.10.

Mrs Thorn. Leith Hospital.

Aet. 70. 20.8.25.

Height 5 ft. 4 in.

Weight 180 lbs.

Normal for age and height = 138 lbs.

Case Record:- Complained of pains in back and side of long duration. Slight tenderness in right loin on deep pressure. Patient very obese; breathless on exertion, complains of "wheezing". Many rhonchi heard on both sides of chest. Requires to get up once or twice each night to pass water. Heart sounds closed and of moderate intensity. Blood pressure: Systolic 170 mm. Hg., Diastolic 120 mm. Vessels palpable. Urine showed albumen.

Blood Sugar.

Time	0	30	60	90	120
Urine	-		-		-
Blood	.157	.200	.227	.21	.175

Here again we have demonstrated, impairment of carbohydrate tolerance, by means of the Blood Sugar curve. This defect might have been missed if urinary examination alone, had been carried out.

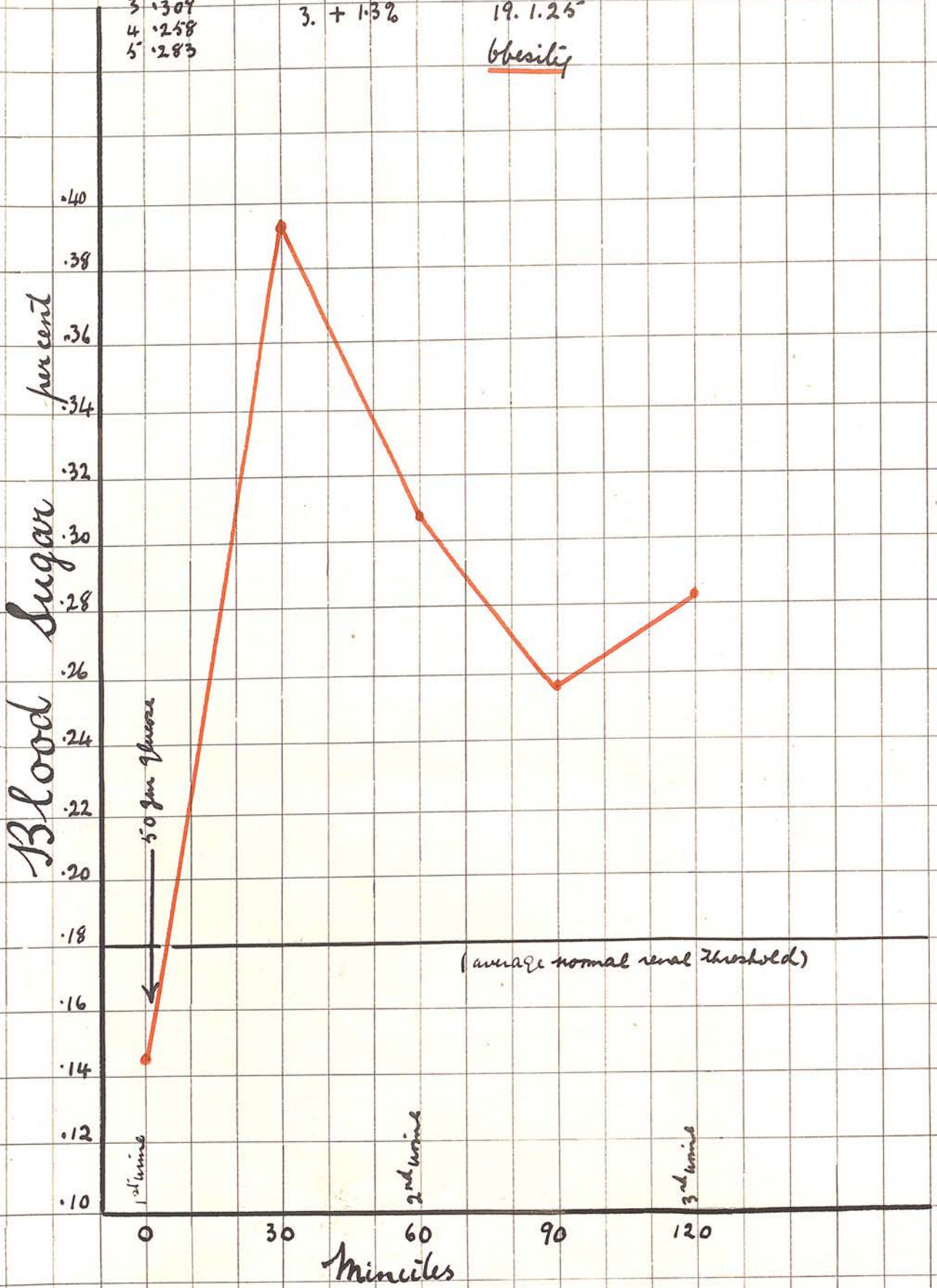
Blood sugar

1 .146
2 .395
3 .304
4 .258
5 .283

Urine

1. 7–
2. 7–
3. + 1.3%

Mrs Hepburn
Royal Infirmary
19. 1. 25
Obesity



GROUP III.

Case No.11.

Mrs Hepburn. Royal Infirmary.

Aet. 45. 19.1.25.

Weight 12 st. = 168 lbs.

Height 5 ft. 6 ins.

Normal weight for age and height = 143 lbs.

Clinical Record:- Complained of pains in back with nothing to account for it. Was of very extreme religious tendencies and belonged to the Plymouth Brethren sect. Became insane after admission and was transferred to Ward 3. Frohlich's syndrome was suspected here and the Sella Turcica was X-rayed, but was reported as normal in size. Urine normal.

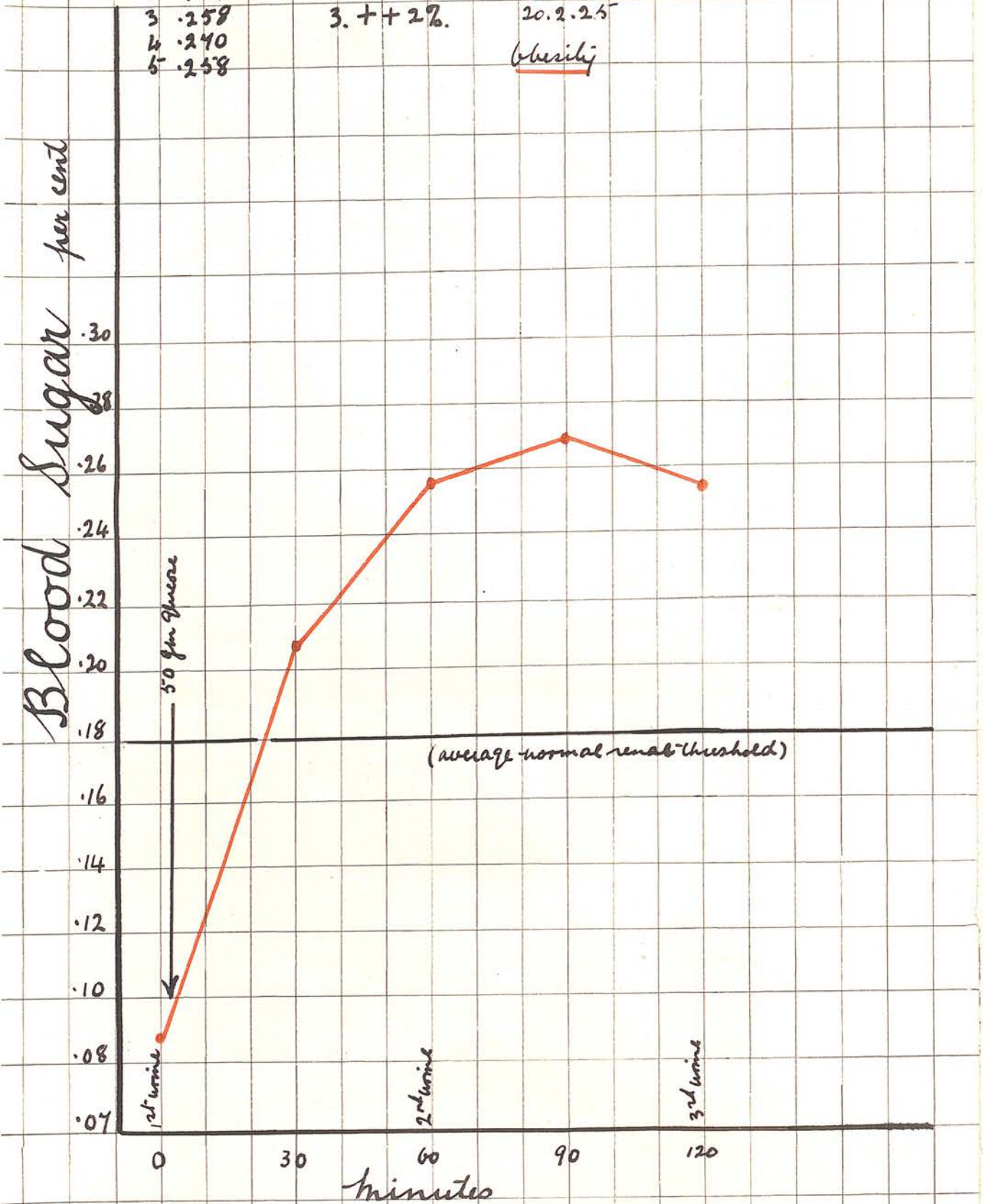
Blood Sugar.

Time	0	30	60	90	120
Urine	-		-		+
B.S.	.146	.395	.307	.258	.283

As far as the type of Blood Sugar curve goes, this case is very like the cases of the previous group. We have a high fasting level, overshooting of the average threshold, prolongation of curve with failure to return to original level after 2 hours, and in contrast to Group II there was a marked reaction for sugar in the urinary specimen obtained after 2 hours. 1.3% was present. (Benedict). This type of reaction is indistinguishable from that given by a Diabetic.

Blood Sugar	Urine
1 ·084	1. ? —
2 ·204	2. + tr
3 ·258	3. + + 2%
4 ·240	
5 ·258	

Mrs Jane Dodds
Royal Infirmary
20.2.25
Obesity



Case No.12.

Mrs Jane Dodds. Royal Infirmary.

Aet. 44. 20.2.25.

Height 5 ft. 2¼ in.

Weight 12 st. 5 lbs. = 173 lbs.

Normal weight for age and height = 129 lbs.

Case Record:- Patient was suffering from neurasthenia. 2 children. Vomiting frequently. Nephropexy in Ward 14 in 1912. One ovary removed 20 years ago. Wassermann - . Evidence of Bronchitis at both bases. Said she suffered from frequency of micturition prior to admission. Urine showed trace of albumen. S.G. 1020. Systolic Blood Pressure 148. Diastolic 100 mm. Hg.

Blood Sugar etc.

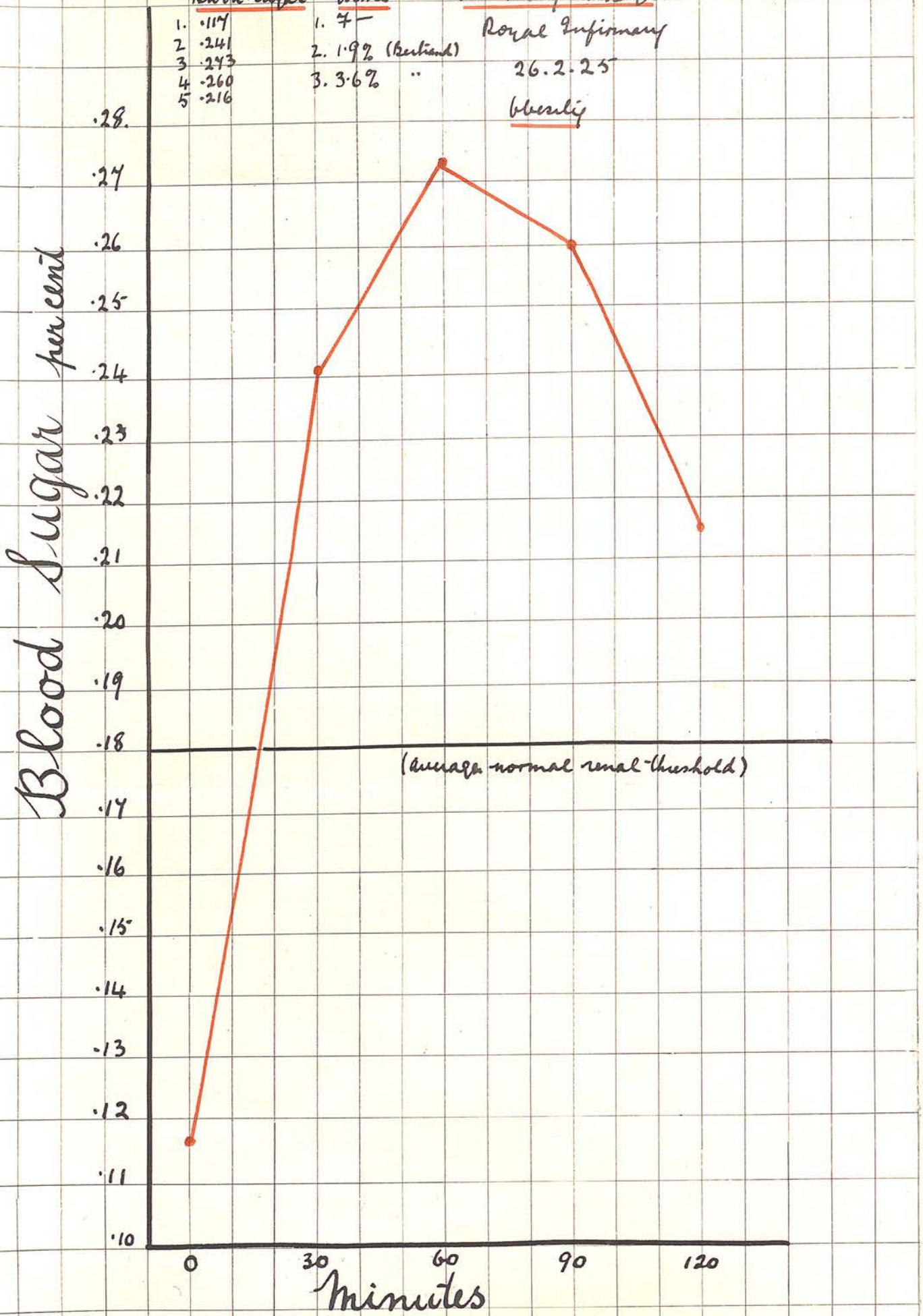
Time	0	30	60	90	120	Minutes.
Urine	-		Tr		2%	Fehling's
B.S.	.087	.207	.258	.270	.258	Gm. %.

This case is essentially the same as Case 11. It shows a diabetic type of curve. The glycosuria is more marked in this case, a trace being shown in the 1 hour specimen and 2% sugar being found in the 2 hour specimen. (Benedict).

Blood Sugar | Urine

1. .114 | 1. 7–
2. .241 | 2. 1·9% (Benland)
3. .243 | 3. 3·6% ..
4. .260
5. .216

Mrs Mary Ramage
Royal Infirmary
26.2.25
Obesity



Case No. 13.

Mrs Mary Ramage. Royal Infirmary.

Aet. 50.

Height 5 ft. 1½ in.

Weight 14 st. 3 lbs. = 200 lbs.

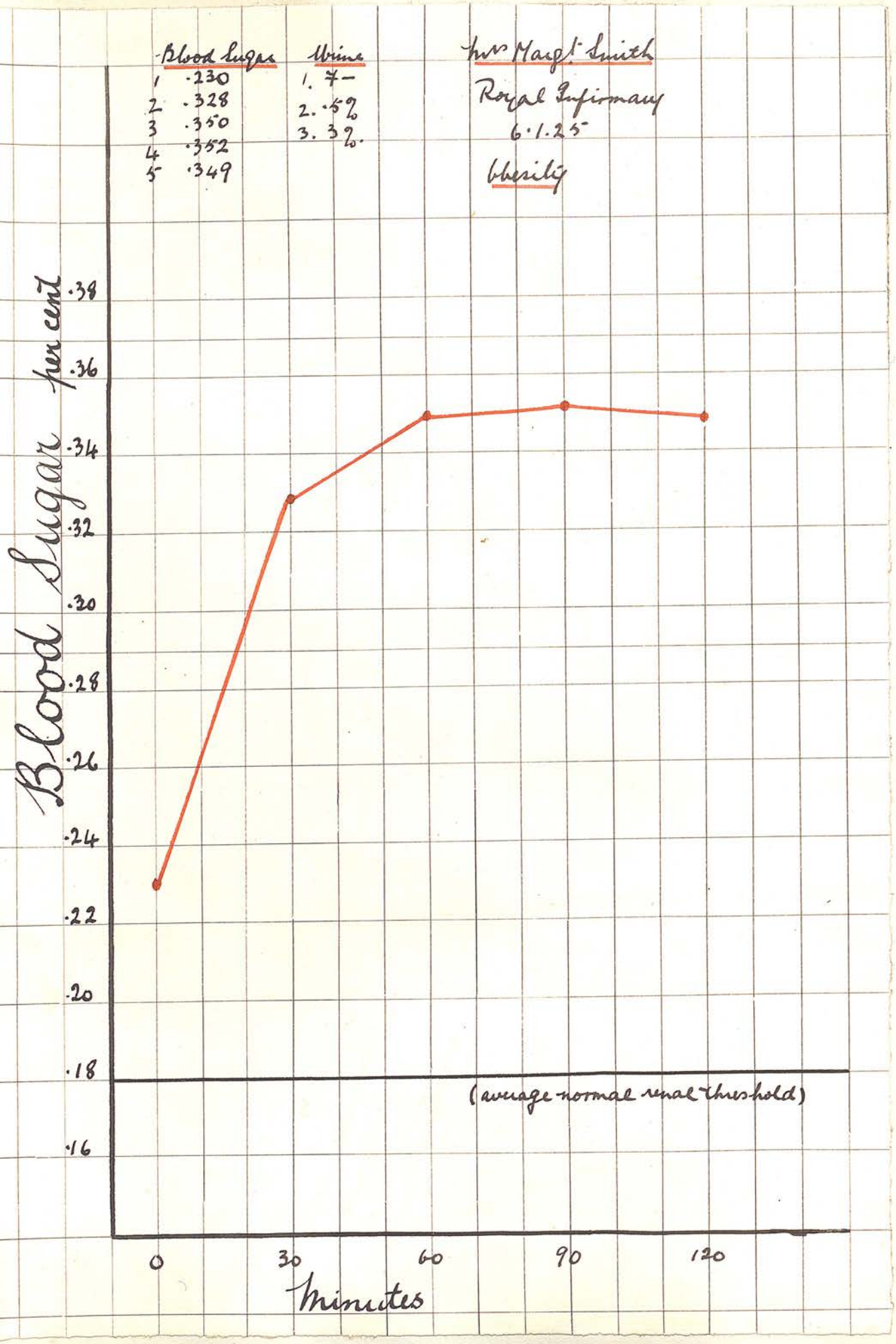
Normal weight for age and height = 130 lbs

Case Record:- Dyspnoea on exertion, and feeling of discomfort in region of heart. Slight oedema of ankles. Systolic Blood Pressure 188. Diastolic Blood Pressure 120 mm. High tension pulse (finger). Heart sounds closed but 2nd sound in aortic area was loud and ringing. Radial artery was palpable at wrist. Trace of albumen in urine. Renal function tests showed slight defect of Kidney function. B.M.R. + 7%. R.Q. .72. Pulse 66.

Blood Sugar etc.

Time	0	30	60	90	120	Minutes.
Urine	-		1.9%		3.6%	Bertrand's
B.S.	.117	.241	.273	.260	.216	Gm. %.

This is another case of the same type as the 2 preceding ones. The Glycosuria was even more marked. The Urinary Estimations were done by Bertrand's method.



Blood Sugar		Urine
1	.230	1. 7–
2	.328	2. ·5%
3	.350	3. 3%.
4	.352	
5	.349	

Mrs Margt. Smith
Royal Infirmary
6·1·25
Obesity

Case No.14.

Mrs Margt. Smith. Royal Infirmary.

Aet. 40. 6.1.25.

Weight 170 lbs.

Height 5 ft.

Normal weight for age and height = 120 lbs.

Blood Sugar etc.

Time	0	30	60	90	120
Urine	-		.5%		3%
B.S.	.230	.328	.350	.352	.349

As far as the Blood Sugar and urinary findings go, this case is in the same category as the previous three. They all show the "diabetic" type of response to the glucose tolerance test. Compare the curves of these cases with those of cases 2 and 15.

Clinical Record:- Complaint of dyspnoea and pain in left side of chest. Diagnosis Rheumatic fever. Wassermann - . 3 pregnancies, 1 still born, 1 abortion, 1 boy living but in delicate health. Father died of Diabetes Mellitus. Systolic Blood Pressure 155 mm. Diastolic 80 mm.

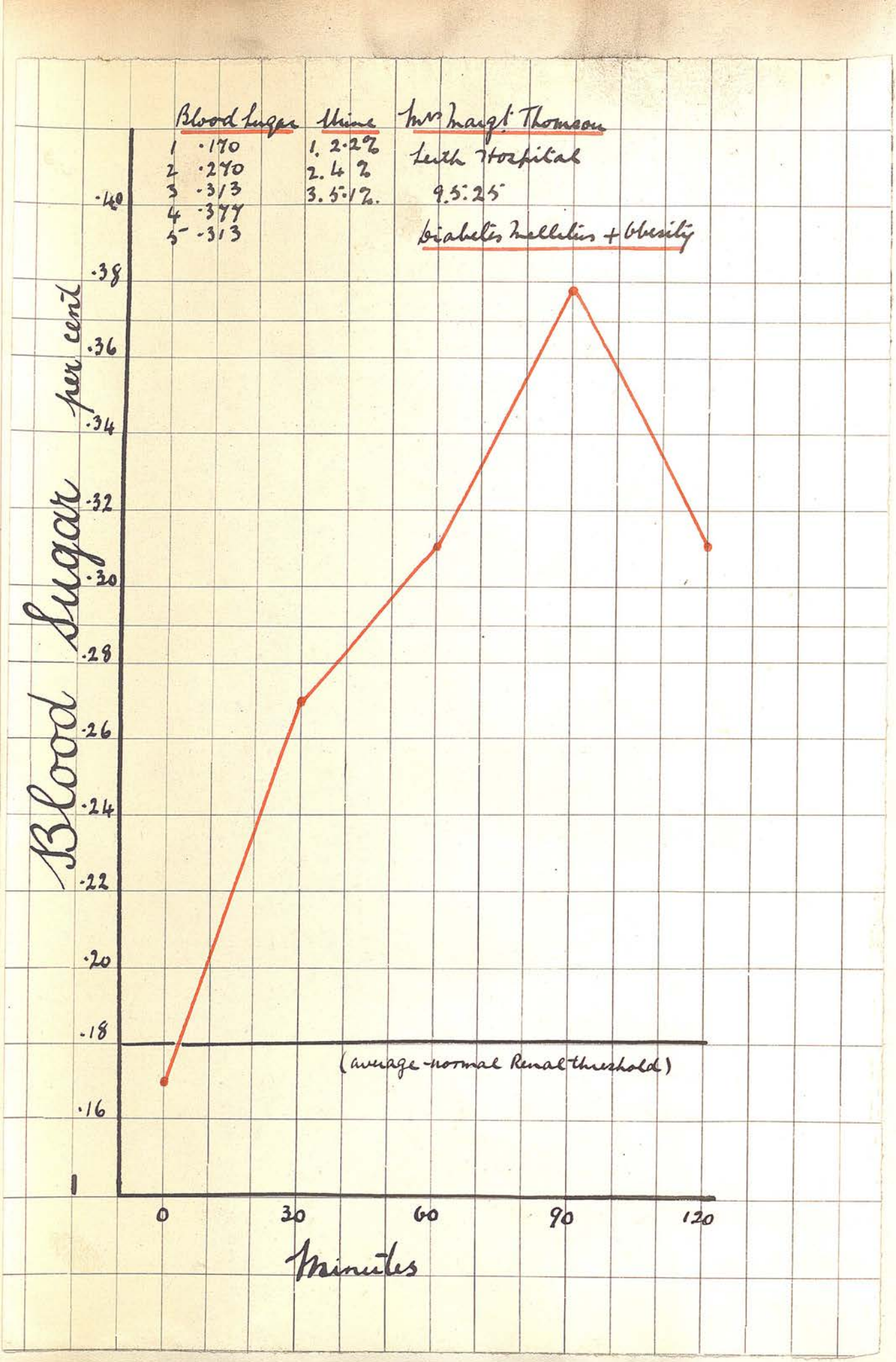
This is perhaps the most interesting case of the whole series. She came into the ward with Rheumatic fever. No murmurs were evident but the joints were very/

very painful and swollen. Pain eased rapidly under salicylates. Glucose Tolerance test was done on 6. 1.25. The "fasting" urine gave a doubtful positive reaction, but this I attribute to the salicylates, which she had been receiving in fairly heavy doses.

The remarkable thing about the case is that she showed a very definite glycosuria in the ordinary 24 hour specimen, each day afterwards; and this did not clear up at all. On 25.1.25 she had a very bad attack of Quinsy, and on the following day the specimen showed more abundant sugar and a definite acetone reaction. In those 3 weeks she had lost a stone in weight. The peri-tonsillar abscess burst on 29.1.25 and she felt greatly relieved.

At the time of appearance of the Acetone she was given 10 units of Insulin at 3 p.m. This was increased to 15 units on the following 2 days and given T.I.D. On 1.2.25 she had only a trace of acetone and no sugar. The insulin was gradually reduced and she was discharged on 13.2.25. on a diet of 2100 calories (C 21) sugar and acetone free. Her weight was now 11 st. 7 lbs. Patient was very much afraid in case she would die "of diabetes like her father", as he was very stout before the onset of the disease.

She was readmitted on 4.3.25 sugar free but with a trace of acetone in the urine. She was suffering from another attack of acute Rheumatism, which again rapidly/


Blood Sugar
Urine
Mrs Margt. Thomson
Leith Hospital
9.5.25
Diabetes Mellitus + Obesity
1 ·170
2 ·240
3 ·313
4 ·377
5 ·313
1. 2·2%
2. 4 %
3. 5·1%.
Blood Sugar per cent
·40
·38
·36
·34
·32
·30
·28
·26
·24
·22
·20
·18
·16
(average-normal Renal threshold)
0
30
60
90
120
Minutes

rapidly cleared up under salicylates. I examined her fasting blood sugar and found a hyperglycaemia of .220%. She was put on a special diet of 1453 calories, and discharged sugar and acetone free, feeling perfectly well.

It would almost seem as if the ingestion of 50 gm. glucose had acted as the exciting cause of a true diabetes in this case. Possibly the cells in the islets of Langerhans which had been struggling for some time past to keep up an appearance of health in the patient, have succumbed to this concentrated dose of Glucose, and given up the struggle. The strain was too much for them. Had the Blood Sugar been examined at an earlier stage in the obesity, the true nature of the trouble might have been realised and further progress towards the complete picture of Diabetes Mellitus, arrested.

Case No.15. Mrs Margt. Thomson. Leith Hospital.
Aet. 41. 9.5.25.
Weight 148 lbs.
Height 5 ft. 2 in.
Normal weight for age and height = 127 lbs

Clinical Record:- This case was admitted from M.O.P.D. as a Diabetes Mellitus with nearly all the cardinal symptoms - boils, thirst, excessive appetite, polyuria/

polyuria, itching, loss of weight, etc. She is included in the series to illustrate that many diabetics are fat to begin with; she was nearly 20 lbs. overweight. She stated that she had been very stout up till about a year ago, since when she had steadily lost weight. On admission she was passing 6% sugar on a diet of 2300 calories. Acetone and diacetic acid were present in fair amount. It is possible that she may illustrate the final result in the progress of the 4 cases in Group III.

Blood Sugar etc.

Time	0	30	60	90	120	Minutes.
Urine	2.2%		4%		5.1%	Benedict's
B.S.	.170	.270	.313	.377	.313	Gm. %.

This curve is typical of Diabetes Mellitus. Note the fasting hyperglycaemia, the overshooting of the curve up to .377%, and its failure to return to the original level. There was sugar present in all three urinary specimens. The fairly large amount present in the "fasting" specimen may be explained as the result of the lowering of the Renal Threshold in early diabetes. This was first shown by C.V. Bailey,[40] who investigated nearly 950 cases of Diabetes Mellitus. He concluded that the Renal Threshold for sugar was lowered in early mild cases, but much raised in severe, long-standing/

long-standing cases. Pickering[41] however states that there is a rather greater proportion of low renal Thresholds among the older cases of diabetes. I rather think however that the fair amount of glycosuria in this case may be due to a lowering of the threshold, as the onset of the diabetes was apparently only a year before admission, and she may be regarded as an early case. She was not by any means emaciated, but actually overweight.

IV. DISCUSSION ON ETIOLOGY AND CLASSIFICATION OF OBESITY.

At this stage I have collected the findings of recent investigations on the subject of the Blood sugar in the obese, and have described the results of my own work on a series of 13 obese patients. It remains now to enquire into Etiology of Obesity, and if possible to make the classification on this basis.

I think that there is now a fair amount of evidence in support of the beliefs of Joslin[5] and Von Noorden,[13] that there is some relation between certain cases of Obesity and Diabetes Mellitus. The careful work of Roth[28] and especially Beeler and Fitz[21] shows that about 25% of obese cases show a reaction to the Sugar Tolerance test indistinguishable from that seen in an ordinary case of Diabetes Mellitus. In my own series of cases, those grouped under III also represent this "diabetic" or shall we say, "pre diabetic" type of Obesity. Case 14 is particularly interesting in that she illustrates the transition stage between the "suspect" cases 11, 12, 13, and the frankly diabetic case 15. It was very likely that she had been hovering on the brink of Diabetes until the ingestion of 50 gm. glucose, by imposing too great a strain on the pancreatic cells, converted her into a permanent diabetic.

The standards used by Beeler and Fitz, Roth, and myself, in adjudging a case to be of a "prediabetic" type were (1) Prolonged type of curve with failure of Blood Sugar to return to the fasting level within 2 hours. (2) Overshooting of threshold. (3) Presence of glycosuria.

It is very evident that, in this type of obese cases, there is a very definite defect in the utilization of sugar. The non return of the Blood Sugar to the original level is due to defective action of the storing mechanism. Besides this defective carbohydrate metabolism, Beeler and Fitz also found in this type some alteration of water excretion. Such cases also excreted a relatively large volume of urine. This has been explained before.

The cases in Group II, according to their Blood Sugar curves, also show a degree of carbohydrate intolerance. Herrick's[17] group of the "Essential Hypertonias" shows a decreased sugar tolerance as well, and its relation to Group III cases, and the relation of both of them to Diabetes Mellitus will be discussed later.

Preble's[19] findings based on investigations in 1000 cases are contradictory to the above views. He gave each of a series of 31 cases a light breakfast and estimated the Blood Sugar 3 hours afterwards. He found the blood sugar in all cases within normal limits./

limits. He does not specify how many gm. carbohydrate his light breakfast was equivalent too. It is doubtful whether such a meal is as good a test of carbohydrate tolerance as the ingestion of 50 - 100 gm. pure glucose.

Preble also found Glycosuria in 7.6% of his cases and stated that this figure shows the incidence of Glycosuria and "presumably of diabetes in obese subjects". He does not state the period between the time of obtaining the urine and the time of the last meal. Also, in these 75 cases he merely tested the urine, not making a simultaneous estimation of the blood sugar at all. I do not think therefore that Preble's findings are very reliable.

A very recent article by Parkes Weber[42] in the B.M.J. may be of interest at this point. It is an attempt to explain the occurrence of great obesity in some diabetics. He says "much has been written on the Continent about the subject of Lipogenic Diabetes in obese subjects. I think that the true explanation is that two metabolic disorders tend to occur in the same individual and appear to run in families. In some cases the Diabetes is grave enough to prevent the occurrence of obesity which would otherwise be present. It is in this way that one can explain the occasional occurrence of obesity in grave cases of Diabetes Mellitus when the latter is successfully kept under by/

by insulin treatment. The insulin prevents the waste due to the chief metabolic defect, and enables the patients to become abnormally fat on a diet of relatively low caloric value. These cases are examples of a latent constitutional tendency to obesity, kept in check by grave Diabetes Mellitus, but becoming manifest when the Diabetes is, so to speak, suppressed by Insulin therapy, which may be of use, indeed, in the treatment of non diabetic emaciated cases of certain kinds."

GROUP IV. ENDOCRINOPATHY.

There is considerable evidence at hand to show that a certain number of obese cases may be the result of an Endocrinopathy. Here again the blood sugar may give some valuable information.

It is well known, thanks mainly to the work of Cushing[30] and Blair Bell,[29] that there is an increased sugar tolerance in Hypopituitarism. By this term is meant that the concentration of sugar in the blood, even after the ingestion of huge amounts of glucose, does not rise very much; and there is, of course, no glycosuria. Therefore a sugar tolerance test might help one to pick out a Fröhlich from among other cases of obesity; a flat curve would be the thing to look for. It must be remembered however that the work of Janney and Isaacson[32] and Zloczower[33], points to the possibility of a clinically identical Fröhlich with a high, sustained, blood sugar curve after ingestion of glucose.

How many cases are traceable to the Ductless Glands it is difficult to say. Preble[19] thinks that they are a rare factor in the causation of obesity. It has been said that the Fröhlich type only constitutes about 2% of all cases of obesity. The work of Wilder and Sansum[27] even denies that there is any increase of tolerance in sugar tolerance in cases

of/

of hypopituitarism. They think that it can be explained by delayed absorption from the alimentary tract.

In spite of recent advances in the state of our knowledge of the ductless glands, it is rather difficult to find out if they play a part or not, in the causation of the more common forms of obesity. Possibly in the future, when our knowledge of the Endocrines, is greater, many of the ordinary cases of obesity may come under the heading of Endocrinopathy. At present, however, Fröhlich's is the only type of obesity, directly traceable to a Ductless gland.

Beeler and Fitz[21] are inclined to class the majority of their cases of obesity as coming under the heading of Endocrinopathy. They showed a comparatively normal blood sugar curve, no glycosuria and a very small or normal excretion of urine. Such cases, in their opinion, do not retain sugar because of an impermeable Kidney, but rather to have some disturbance in Sugar and Water Metabolism, which may be related to an Endocrinopathy. It seems possible that such patients burn or store sugar with unusual rapidity, a reaction which may have a sparing influence upon fat and protein metabolism and may be a factor in the development of the adiposity. Such people, they say, are not likely to develop diabetes, and should be treated for Obesity and an Endocrine lesion if such be demonstrable.

In/

In cases of Myxedema we have also an increase in bulk of the subcutaneous tissues, but this is not a true obesity. The increase of the so-called "fat" is restricted to certain areas, e.g. shoulders, buttocks, back, etc. The new tissue, however, is not fat at all, so it is not necessary to consider further the relationship of Myxedema to Obesity.

Leonard Williams[43] states that in some women the prolonged strain of pregnancy has the effect of unduly exhausting the thyroid, and they are unable to suckle the child, for lactation is dependant on a due supply of thyroid secretion.[44] Such women generally become obese and lethargic and remain so for varying periods until the gland has had time to recover itself.

According to de Wesselow[16] cases are certainly met with in which obesity of the pituitary type, often dating from pregnancy, is associated with marked hyperglycaemia and the passage of large quantities of sugar in the urine, but in which the symptoms are in no way suggestive of a progressive diabetes of pancreatic origin.

Before leaving the question of the part played by the Ductless glands in obesity, and their effect on the blood sugar in that condition, I wish to mention, in more detail the group of cases referred to by Herrick[17] as the "Essential Hypertonias".

Herrick,/

Herrick, for several years, investigated the inter-relation of hyperglycaemia and high blood pressure, and concluded that the majority of the cases belonged to a quite definite group characterised by four cardinal symptoms, i.e. Hypertension, arterio-sclerosis, hyperglycaemia and obesity. While it does occur, he states, it is rare that Hyperglycaemia is found in a thin person associated with Hypertension. This group he terms the "Essential Hypertonias", and it does not include the examples of hypertension that are associated with other definite conditions such as Kidney insufficiency, aortic incompetence, toxaemias of pregnancy, thyroid disturbances and intra-cranial pressure. The Essential Hypertonias comprise 10-30% of all cases of Hypertension.

Herrick explains this syndrome as the result of a faulty and ill-balanced diet with an excess of carbohydrate in a person in middle life with Hypertension. If the carbohydrate tolerance is below normal there is an almost certain strain of the cells of the pancreas and a tendency to the development of diabetes. There results also, an increase in weight and arterio-sclerosis with a further rise in blood pressure. He stresses the fact that arteriosclerosis and hyperglycaemia are not mere casual associates and that even in juvenile diabetes some arterial thickening/

thickening is very common, while in diabetes of later life it is very constant. If we agree with Herrick's views then it would have been more logical to put the Essential Hypertonias under the previous group (pre-diabetic).

Herrick is not the only observer to note the relationship between hypertension and hyperglycaemia in cases without any definite kidney lesion. Neubauer,[45] O'Hare,[46] and Harle[47] have also recorded it. The last worker stated that in 25% of cases with hypertension without apparent kidney lesion, there was definite hyperglycaemia. In another 25% the blood sugar was at the upper limit of the normal.

Botti[48] also found that in the presence of hypertension the blood sugar was increased and sugar tolerance lessened. Kylin[49] has also described the association of lowered carbohydrate tolerance with hypertension and further states that there is an increase of uric acid in the blood of this type of case. He does not think however that such cases are diabetic in tendency. Hamman and Hirschman[50] find also, that hypertension is an important sign of a disturbed carbohydrate metabolism.

It appears, then, that Herrick's Group of the Essential Hypertonias, with its leading features of obesity, hypertension, arteriosclerosis, and hyperglycaemia, is definitely established. I would point out/

out at this stage that there is no "apparent" kidney lesion. My reason for including such a group under Endocrinopathy, is that Neubauer[45] suggested that excessive activity of the Supra-renals was the underlying factor: and Hamman and Hirschman[50] were also tempted to find a common explanation for the hypertension and hyperglycaemia, in altered Epinephrin function.

They however, as a result of their investigations were forced to conclude that the action of Epinephrin on sugar metabolism is independent of its other action; that there is no constant relation between its vascular effects and the hyperglycaemia and diuresis. Epinephrin has no effect upon the Renal permeability for glucose. Their conclusions are in agreement with those of Botti[48] and Härle[47] who could establish no relation between the degree of hypertension and the level of the sugar in the blood.

It is of interest to note that Rose[51] finds that decline in weight is almost always accompanied by a fall in blood pressure, particularly when this was previously high. Herrick[17] confirmed this in his cases, and found also that the reduction of the Blood sugar to normal and its maintenance there, was followed constantly by a decline in blood pressure. He does not think that this is direct cause and effect, but is a consequence of the reduction in body bulk

which/

which quite constantly follows the dietary regulation of high blood sugar in the obese. Mosenthall[52] also suggested that the decline in blood pressure observed to follow reduction in blood sugar in the obese, was merely the result of undernutrition causing loss in weight.

Up to this point the discussion has centred mainly round those cases of Obesity showing a carbohydrate metabolism, altered in one or other of two directions; a group, called "pre-diabetic", in which the carbohydrate tolerance is definitely lessened; and a group classified under Endocrinopathy, in which the carbohydrate tolerance is generally believed to be increased, though this is disputed by Wilder and Sansum. It is very difficult to allot the part played in carbohydrate metabolism by the ductless glands, at least as far as obesity is concerned. Beeler and Fitz rather favour classing 75% of their cases under Endocrinopathy. Preble thinks they play a very minor part in obesity; and Wilder and Sansum deny any increased tolerance in Hypopituitarism. Such contradictory statements cause much confusion in the classification of the subject.

Then again it is difficult to allocate which group the Essential Hypertonias should really belong to. I described them under Endocrinopathy, but as they/

they show a decreased carbohydrate tolerance, they ought really to come under Group III more than Group IV. Yet I hesitate to say that they bear the same intimate relationship to Diabetes Mellitus as do the cases I have described under the pre-diabetic group.

METABOLISM IN OBESITY.

Let us look now at the cases of Obesity which can neither be classed as pre-diabetic, or "Endocrinopathic". These probably constitute the great majority of cases. While it is admitted that, in certain cases, obesity may result in spite of a properly balanced diet and well regulated exercise, and, that in these cases, the condition is due to a metabolic error, the bulk of opinion favours the view that obesity in most instances arises from a disproportion between the amount of energy taken in as food and the amount expended by the body.

Most people follow von Noorden's[53] classification of obesity in which he describes two types (1) a normal metabolism with adiposity arising from increased food intake and or decreased energy expenditure and (2) a true slowing of metabolism. There is abundant evidence in favour of the first[54] heading but little in support of the second. Van Noorden says "that it is an undoubted fact that certain fat persons show

a/

a tendency to get fatter in spite of an intelligent regulation of diet and exercise, and others fail to lose weight when taking a low caloric diet over a long period of time. These facts suggest that an abnormal metabolism is the true cause of the condition."

Means[55] carried out observations on the B.M.R. of 12 cases of obesity using the Benedict apparatus and the Du Bois formula and found that there was no departure from the normal Basal Metabolic rate in such cases. Strouse[56] and Dye made an exhaustive search through the literature in an attempt to discover the relation between food intake and weight in some obese persons and concluded that obesity can and does occur without showing any direct relation to food intake. Conducting a further series of investigations into the Basal Metabolic rate in obesity, they found that excessive overweight was not associated with any constant change in Basal metabolism and that the condition cannot be caused by any changes in Basal Metabolism. Preble[19] records the results of work done on the B.M.R. of 39 cases: 21 were slightly above the normal standard and 18 slightly below, i.e. the variation from the standard is about equal each way. He thinks that he is justified in assuming that the basal metabolism in the obese is within normal limits, and that the ductless glands are rarely an etiological factor. Eason and Whitridge Davies[57] in a paper on the B.M.R. in Hyperthyroidism, recorded the B.M.R. in/

in a few cases of obesity and Hypopituitarism, and such results appeared to be within normal limits.

Roaf[58] states that by the conversion of sugar into fat a more concentrated form of energy is produced. During the process carbohydrate is reduced, and the oxygen derived from the carbohydrate is used to oxidise other carbon compounds with the result that the carbon dioxide will appear in the expired air without a corresponding absorption of oxygen. The R.Q. is the resultant of all the oxidative processes in the body; an R.Q. greater than 1 must be due to the conversion of carbohydrate into fat. The reverse condition, i.e. conversion of fat into carbohydrate would give a low R.Q. But it has never been proved that fat can be changed into carbohydrate.

Lovat Evans[59] in dealing with the utilisation of foodstuffs states that Krogh and Lindhard found that subjects fed on a fat diet were much more easily fatigued than those fed on a carbohydrate diet. When the subject passed from rest to a state of muscular work the R.Q. was raised if it had previously been low, but lowered if it had previously been high. They suggest that the proportion of fat to carbohydrate used, whether at rest or at work, depends upon the available supply of both; when the diet consists chiefly of fat (R.Q. below 0.8) there is a constant conversion of fat into carbohydrate which is provisionally stored; while when the R.Q. is above 0.9 carbohydrate is being transformed into and stored as fat.

I wish now to make a few more direct references to the condition of the Fat Metabolism in Obesity. My main purpose in this paper was to investigate, rather, the state of carbohydrate metabolism, but as this necessarily implicates the metabolism of Fat I shall mention one or two points on this subject, out of the literature.

Howell[54] suggests that while the resting B.M.R. in fat and thin people may be alike, it is possible that a diet in excess of this may be handled differently in the two cases. In one the excess may be destroyed by the active tissues, while in the other the fat tissues may claim a share. He points out that very little is known of the special physiology of the fat cells themselves. Any small difference of this kind in the action of the adipose cells would have a cumulative effect which would suffice to explain a tendency towards the laying on of fat.

Waldwogel[60] believed that in adiposity there was some disturbance of the intermediary fat metabolism by which β (beta)-oxybutyric acid was not burned to its usual completion.

In this connection, note the conclusions arrived at by Folin and Denis[61] as a result of their experimental investigations: They state that Obesity is not a predisposing or contributing factor in the onset or intensity of the acidosis of starvation. The total acetone/

acetone excretion with the breath in starvation is quantitatively insignificant (at most 1 gm. per day) and the notion current among Clinicians that they can "smell acetone all over the room" when a case of acidosis is present is quite erroneous.

By repeated fasts of moderate duration the obese acquire an increased ability to starve without the production of acetone bodies. They lose less body protein than others in the course of moderate periods of starvation (4-6 days) and on repeating the fasts the losses of body protein become still smaller. Successive moderate periods of starvation constitute a perfectly safe, harmless and efficient method for reducing the weight of those persons suffering from obesity.

Let me refer once again to the Carbohydrate metabolism. Rosenfeld[62] pointed out many years ago that there was reason to believe that the carbohydrates are more easily and more quickly destroyed in the body than the fat, and that therefore the latter may be more quickly and more readily deposited in the tissues. An excess of carbohydrate, however, beyond the needs of the body, will also be preserved in the form of fat or glycogen. This belief is now widely held and Beeler and Fitz state that the probable cause of obesity in most cases is the fat sparing action of the carbohydrate element in the diet.

Briefly,/

Briefly, then, we have seen that there is apparently no change in the B.M.R. in the obese; that Fat metabolism is normal in the obese (Folin and Denis); deficient (Waldwogel) or is altered through some change in the special physiology of the fat cells themselves (Howell); and finally that the production of the obesity, in the majority of cases depends upon the fat sparing action of carbohydrate.

There appears therefore to be some doubt about the state of Fat metabolism in the obese subject. Now comparatively little is known about fat metabolism even in the normal subject. The source of fat is from the pre-formed fats of the blood and also from the carbohydrate of the food. The latter however also acts as a fat sparer. It has not been proved that fat can be converted into carbohydrate. During starvation the fat in the fat depots is used by the tissues after having been desaturated in the liver by the removal of hydrogen. These unstable fatty acids are carried to the muscles and other tissues in which they enter the complex protoplasm of the living cells and are finally oxidised to CO_2 and water.

But the point which is of interest in the discussion of the Fat metabolism in the obese, is the well known dependence of Fat metabolism upon that of Carbohydrate. In the presence of a faulty carbohydrate/

carbohydrate metabolism, fats are incompletely burned, and acetone and diacetic acid are produced. Using MacLeod's[64] metaphor "Fat is a much less easily oxidised substance than glucose, and it requires the burning fire of sugar to consume it. If the carbohydrate fire does not burn briskly enough it smokes, i.e. the fat is incompletely burned and the smoke is represented, as it were, by Ketones and derived acids." This is the general view adopted in describing the association of the two metabolic processes. Parkes Weber,[42] it will be recalled, suggests that in obese people and obese diabetics, both metabolisms may be defective at the same time and quite independently of each other.

A possibility then, which should be kept in mind, is that in those cases of obesity, where a decreased carbohydrate tolerance has been established, there is very likely to be some disturbance also of the fat metabolism. This would be in support of Waldwogel's view. It is possible, of course, that the Fat metabolism might not be affected until the defect in that of Carbohydrate had reached a certain degree of severity. I have not been able to get information on this point.

We have returned then to the question of the carbohydrate tolerance in the obese. This has already been discussed in some detail, and a very brief refer-

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reference is all that will be required. Beeler and Fitz, and Roth have recorded a "pre-diabetic type" of obesity and the cases investigated by myself and placed in Group III appear to be identical with this type. Such cases show a very definitely impaired carbohydrate tolerance; after the glucose tolerance the urine of case No.14 showed very definite reactions for acetone and di-acetic acid. Unfortunately the acetone and diacetic acid tests were not carried out in the other cases of this group, after the glucose tolerance test was completed. As far as can be made out from the small amount of work done on this subject, cases of this "pre-diabetic type" constitute about 25% of all cases of obesity.

A much smaller number of cases come under the heading of Group IV, i.e. Endocrinopathy. They, in general, show the Frohlich's syndrome, and an increased sugar tolerance; the fat in the food is spared and accumulates rapidly in the subcutaneous depots. Such cases are thought to come to about 2% of all cases. There is no defect of fat metabolism in such cases.

The majority of obese people show nothing wrong either in their carbohydrate or fat metabolism. Such cases as I have investigated myself, I have placed in Group I. All of Preble's series of 31 cases, and 75% of Roth's and Beeler and Fitz' series showed no abnormality/

abnormality of their blood sugar.

I must however make special reference again to the Essential Hypertonias of Herrich. His work as far as the association of Hyperglycaemia with Hypertension is concerned is in full agreement with that of Neubauer, Härle, O'Hare, Botti, Kylin, Hamman and Hirschman. As Hypertension is a very common associate of obesity, this discovery is of considerable importance. In Preble's series of 1000 cases, every one had a raised blood pressure; this was especially evident in those cases over 30 years of age: 62 cases out of the 1000 had a blood pressure of over 200 mm. systolic. Herrick did not do a Sugar Tolerance test on his cases, but simply investigated the fasting level of the Blood Sugar; the latter varied from .160 gm.% to .250 gm.%.

There is, I think, more than a possibility that the Essential Hypertonias may be related to those cases which I have placed in Group II, and which all showed albuminuria, raised blood pressure, and considerable overweight. The absence of Glycosuria in the presence of marked hyperglycaemia was presumably due to a raised renal threshold, a condition which is constantly present in cases of Chronic Nephritis. There is abundant evidence on this point. Graham[37-39] states that hyperglycaemia without glycosuria occurs in Nephritis. He has observed many cases of raised renal/

renal threshold, and 0.300 gm.% was the highest level of Blood sugar recorded without any glycosuria being present.

De Wesselow[65] says that the existence of nephritis appears to reduce the permeability of the Kidney to sugar and that absence of sugar from the urine is therefore not a definite proof that the blood sugar is within normal limits. "In some cases of chronic interstitial nephritis and in patients suffering from arteriosclerosis and hypertension the blood sugar may be found to be abnormally high. This hyperglycaemia is not infrequently associated with a raised renal threshold for glucose and no glycosuria results." He regards the hyperglycaemia as the result of general vascular changes resulting in fibrosis in which the islands of Langerhans participate.

Spence[66] regards the hyperglycaemia referred to in Nephritis as merely the expression of the decreased tolerance for carbohydrate found in old age.

According to Hopkins[67] Hyperglycaemia occurs in many high pressure nephritic cases and not in low pressure ones, and Hamman and Hirschman[50] say that many cases of nephritis have a high renal threshold so that though the blood sugar may exceed .20 gm.% only a trace or no sugar at all appears in the urine.

Hypertension with or without nephritis must occur in a considerable proportion of obese people. As was noted/

noted above, it was present in all of Preble's 1000 cases; and evidence of Kidney impairment was found in 463 cases out of the 1000. Herrick and other writers have pointed out the increasing tendency towards arteriosclerosis in the obese. We have seen that in nephritis there is some decrease of Sugar tolerance and I have appended a few cases in Group II showing obesity, albuminuria, hyperglycaemia, with a blood pressure rather on the high side.

I repeat that there is very much in common between the type of cases described under the Essential Hypertonias, and the class of case which I have placed in Group II. It is quite possible that they are actually identical. It is difficult to argue that; if a patient has hypertension and arteriosclerosis, he has no impairment of Renal function - chronic interstitial nephritis and arteriosclerosis go hand in hand. Herrick stated that his cases had no "apparent" kidney involvement. It is quite likely, I think, that there is a common explanation for the two classes.

Such an explanation is however rather difficult to find. As mentioned above, de Wesselow[65] suggests that it is not due so much to the renal lesion, but to widespread arterial changes, involving among other vessels, those supplying the Pancreas. O'Hare[46] also put forward the theory of pancreatic arteriosclerosis as being at the root of the condition. Pearce and Keith[68]/

Keith[68] think that; because a diseased Kidney is unable to utilise the ordinary amount of sugar, diminished sugar consumption results with accumulation of this substance in the blood. Meyers and Killian[69] noted the increase of the diastatic activity of the blood in nephritis and suggest that this might account for the hyperglycaemia. Botti[48] thinks that "the decreased sugar tolerance seen in cases with hypertension, may be due to delayed metabolism, lessened functional capacity of the liver, or disturbance of the General Circulation.

Perhaps the following observation of Hamburger and Brinkman[70] may have a bearing on this point. Those two authors working on the kidney of the frog, found that, by varying the amounts of Calcium and Potassium in the perfusing fluid, and making the H ion concentration the same as that in frog's blood, they have been able to show that dextrose is not excreted in the urine whereas all the other sugars are. These experiments show that the Renal threshold is different from[71] the various sugars and can be altered for dextrose by altering the character of the perfusing fluid.

It is known that in Nephritis:- there are slight variations in the amount of the Serum Potassium, Calcium[74] and Magnesium. There is a great decrease in all cases of Nephritis showing oedema and in all cases/

cases of the Azotaemic type. Is there any relation between this observation of Hamburger and Brinkman, and the factors causing the rise of the renal threshold in Nephritis?

Are we now in a position to explain the obesity and the hyperglycaemia in the "Essential Hypertonias" and in the Group II cases?

Obesity usually has a very small beginning. It probably originates in faulty regulation of diet and exercise. Overeating or too large a proportion of carbohydrate and fat in the diet gives too much energy for the needs of the body. The surplus is stored in the fat depots as fat. The amount of fat, able to be ingested at a meal, is strictly limited, and the result is that the usual fault in the diet is the excess of carbohydrate. The protein is used for tissue repair and what is left over usually joins the fat and carbohydrate katabolic chains, and thus goes to swell the excessive amount of these substances in the diet.

Carbohydrate is the great energy provider in the diet and is more easily and more rapidly burned up than Fat. The result is that when it is in excessive amount in the diet, it is burned in preference to the fat and acts as a fat sparer. The bulk of the ingested fat is then carried to the fat depots and stored there. According to Beeler and Fitz[31] and Rosenfeld,[62]/

Rosenfeld,[62] the adiposity in obese subjects is wholly due to this fat sparing action of the carbohydrates which is the main factor in the obesity. Clapp thinks that it is due to the direct conversion of the glucose in excess of the energy requirements into fat. This can occur, of course, and there is abundant physiological[71 & 54] evidence to show that carbohydrates can be converted into fat. Lawes and Gilbert, by their historical experiments on feeding pigs, were the first to prove it. It probably does occur to some extent in obesity but I doubt if it is the main factor.

Persistence in this faulty diet and faulty regulation of exercise will lead, sooner or later, to a considerable increase of weight, and as the weight increases, the individual becomes less able and less inclined for exercise and so the vicious circles begin. The patient gets fatter through lack of exercise, and with the increase of weight there is increase in the volume of blood, and increase in the blood pressure. The circulation of this increased volume of blood means an extra strain upon the heart, and the raised blood pressure tells back upon the heart, kidneys, vessels, etc.

With a high blood pressure, as has been shown, we have associated an hyperglycaemia, and, it is said, that this betokens some defect in carbohydrate metabolism. If the diet be not attended to, the excess of/

of carbohydrate ingested throws a still greater strain upon the pancreatic cells (and possibly a tendency towards the development of diabetes). Then there is the almost certain further rise in weight and blood pressure, and an accelerated tendency towards the development of arteriosclerosis, probably due to the hyperglycaemia: in severe diabetes arteriosclerosis is constant. Impairment of renal function is very likely to appear from the continued high blood pressure and the arteriosclerosis. We have now reached the stage represented by the cases in Group II and very likely by the Essential Hypertonias.

Whether such cases are likely to go further and develop a true diabetes, it is difficult to say. I somehow think not, and would hesitate to classify them with the "Pre-diabetics". The possibilities are that death may occur from the cardio-vascular condition, before diabetes manifests itself clinically. It is a common belief, that, whenever high blood pressure or chronic interstitial nephritis is diagnosed, protein should be eliminated from the diet as far as possible. The deficiency in the diet is then mainly compensated by the addition of carbohydrate, as the amount of fat that can be comfortably ingested is limited.

This line of treatment in obese people with hypertension and/or azotaemic nephritis, would seem, in view/

view of what has just been said, to be irrational. It simply means aggravating the condition and straining the pancreatic cells further.

Herrick, de Wesselow, and O'Hare all think, that in these cases of hypertension, associated or not with nephritis, there is some loss of carbohydrate tolerance and various explanations are put forward. Herrick used the fasting hyperglycaemia as evidence enough, for carbohydrate intolerance; it would have been interesting to see how his Essential Hypertonias responded to a Glucose tolerance test, and how such a response would have compared with the cases in Group II. The cases in that group had in common with the Essential Hypertonias, a high blood pressure, hyperglycaemia, obesity and cases 7 and 10 had arteriosclerosis also. The blood sugar curves of all the cases in this group resemble that of diabetes, in that they show (1) high fasting level, (2) prolongation of curve, (3) failure to return to original level in 2 hours. There was no glycosuria demonstrable by the ordinary test. We must assume therefore that such cases show a lessened carbohydrate tolerance and that glycosuria is prevented by a raising of the renal threshold. Both conditions may arise from the high blood pressure, or nephritis or both.

In case No.6, if recovery from the acute nephritis, from/

from which she suffered, was incomplete we would find that she would merge into a chronic nephritis, and would ultimately develop the changes described in connection with Group II. It was difficult in this case, to get at the true original weight. She merely said she was stout before the onset of the nephritis. In spite of the Fasting hyperglycaemia I placed her under Group I as she shows a well functioning storage mechanism, though it rather resembles the "lag" type.

The other cases in Group I show a perfectly normal Blood sugar curve. Case No.5 shows a "lag" type of curve which according to MacLean is of no significance. Their respective weights were 164, 145, 166 lbs. The normal weights for the same age and height were 137, 135, 130 lbs. The cases were therefore 7%, 11%, and 22% overweight, respectively. The average weight of the group was 158 lbs.

The explanation of the obesity in such cases as these is probably a simple disproportion between the intake and output of energy, i.e. too much, or ill-balanced, food without proper exercise; all give histories of sedentary habits. It is quite possible that if such people persist in such dietetic errors and ill regulated exercise, the obesity will be gradually aggravated until the vicious circle appears, when the tendency will be greatly accelerated.

With the onset of Hypertension, Hyperglycaemia, and/

and arteriosclerosis, and nephritis, they come now under Group II where there is some loss of Carbohydrate Tolerance. As mentioned above, it is questionable where the pre-diabetic cases in Group III represent a later stage than cases in Group II, or the Essential Hypertonias. Yet the only differences between the two groups are that there is no glycosuria in group II, and albuminuria was not so evident in group III.

What happens to all the sugar circulating in the blood in such cases?. Most of it will be stored, in time at least, by the defective storage mechanism. Some of it will be oxidised. In true diabetes mellitus there is not only a defect in storage, but also defective oxidation as well. The cases in Group II resemble Diabetes mellitus in that storage appears to be defective. Unfortunately I have not any information about the R.Q. of cases in this group. Normally, after ingestion of glucose one would expect to find a slight rise in the R.Q., owing to the oxidation of the carbohydrate. If in cases such as those in Group II, it was found that the R.Q. was low, that would be additional evidence in favour of an impaired carbohydrate metabolism. As far as Basal metabolism is concerned there is not any change from the normal in an obese patient.

There/

There is also the possibility that the excess of sugar circulating in the blood may be converted into fat in those patients, as such a process can and does occur. This would aggravate the tendency towards laying down of fat caused by the other factors mentioned before. The R.Q. under such circumstances would again be high.

There are two other references I wish to make with regard to the state of the blood sugar in the obese. One is that of MacLeod[72] who states that "many cases of hyperglycaemia and glycosuria which are ordinarily supposed to be due to different causes, may really be asphyxial in nature." In all the cases in Group II and in Cases 13 and 14 in Group III, cyanosis, dyspnoea, fainting and wheezing were all present. It is doubtful however, whether such features were present in sufficient intensity, to produce the degree of non-aeration of the blood, necessary to produce the hyperglycaemia of asphyxia.

The other reference is to the work of Cajori Crouter,[73] and Pemberton[74]. It has been known for some time that different people respond variously to the 100 gm. sugar tolerance test. In some the resultant hyperglycaemia is associated with Glycosuria, but in others there may be no glycosuria. The exaggeration and prolongation of the hyperglycaemia seen in people with a low sugar tolerance has been put down to a deficiency/

deficiency of insulin, which is depended upon to remove sugar from the blood. The recent investigations of the above workers however show that there is another possibility to be considered.

Since muscle tissue seems to be a prominent site for removal of sugar from the blood, interference with the blood supply to muscle tissue, might be expected to alter the rate at which sugar leaves the blood. Cajori, Crouter, and Pemberton find that by interfering with the blood supply to large muscle masses through elevation of the legs and one arm, an exaggerated and prolonged hyperglycaemia can be induced in some persons.

These facts are interpreted as indicating that the rate at which sugar leaves the blood after glucose can be influenced by the character of the blood supply to tissues active in sugar removal. Such mechanical factors should be taken into consideration in the interpretation of a low sugar tolerance.

S U M M A R Y.

1. A Sugar Tolerance test gives information of great value for the accurate diagnosis and treatment of an obese patient.

2. About 25% of obese subjects show a response to the glucose tolerance test indistinguishable from that found in a definite case of diabetes mellitus. Such cases, though not as yet showing the characteristic clinical signs of diabetes, should be regarded as mild diabetics and treated as such. If left untreated they will, in all probability, ultimately become true diabetics.

3. A small proportion of obese cases are the result of an Endocrinopathy, e.g. Fröhlich's syndrome, "post-pregnant" obesity (from exhaustion of the thyroid). The blood sugar shows a poor response to the glucose tolerance test, and the probable cause of the laying on of fat is the fat sparing action of the carbohydrate of the food.

4. There is a second type of obesity in which decreased sugar tolerance is a prominent feature. It again may be sub-divided into two groups.

The 1st Group is characterised by obesity, high blood pressure, hyperglycaemia, and evidences of/

of Renal impairment. The blood sugar curve is exaggerated and prolonged; there is no glycosuria associated, this being due to a raised renal threshold (probably a result of chronic interstitial nephritis.).

The 2nd Group is the "Essential Hypertonias" characterised by arteriosclerosis, hypertension, obesity, and hyperglycaemia. They differ from the above group in having no evidence of Kidney involvement. They show a fasting hyperglycaemia.

Both types probably admit of a common explanation and both show evidence of impaired carbohydrate metabolism. Their relation to the "prediabetic" Group III is as yet uncertain. Their relation to diabetes mellitus seems to be more distant than that of the above Group III. This group with hypertension and nephritis, or hypertension and arteriosclerosis, associated with hyperglycaemia and obesity, probably includes about 10% of all cases of Obesity.

5. About 60-70% of Obese subjects have a comparatively normal blood sugar concentration, and respond in a normal manner to the sugar tolerance test. The obesity in such cases is probably due to a simple disproportion between energy intake and expenditure.

6./

6. It is possible that the above type of case may progress until hypertension, nephritis, arteriosclerosis start their vicious circles, and force the case into Group II.

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